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Comprehensive Care in Clinical Trials Legislative Language

To amend the act entitled "Federal Food, Drug, and Cosmetic Act" to authorize the Food and Drug Administration to require psychosocial distress screening and follow-up for patients in clinical trials for drugs and biological products.

SECTION 1. SHORT TITLE.
This Act may be cited as the "Comprehensive Care in Clinical Trials".

SEC. 2. PSYCHOSOCIAL DISTRESS SCREENING and FOLLOW-UP FOR DRUGS AND BIOLOGICAL PRODUCTS.
IN GENERAL.—Subchapter A of chapter V of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 351 et seq.) is amended by inserting after section 505(E) the following:

''SEC. 505F. PSYCHOSOCIAL DISTRESS SCREENING and FOLLOW-UP FOR DRUGS AND BIOLOGICAL PRODUCTS. "(a) NEW DRUGS AND BIOLOGICAL PRODUCTS.—
"(1) IN GENERAL.—A person that submits an application (or supplement to an application) for a drug intended for use in the diagnosis, cure, mitigation, treatment, or prevention of a serious or life-threatening disease or condition for which treatment is required on a recurring basis— "(A) under section 355 of this title for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration, or "(B) under section 262 of title 42 for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration, may submit with the application the psychosocial distress screening and support plan described in paragraph (2).

"(2) PSYCHOSOCIAL DISTRESS SCREENING AND SUPPORT PLAN.—The psychosocial support plan referred to in paragraph (1) shall contain a record of— "(A) The screening of all patients in any clinical trial initiated on or after January 1, 2017 of any such drug or biological product described in paragraph (1) for psychosocial distress risk using a validated measuring scale designed to assess the psychosocial needs of patients enrolled in the trial, including each patient's ability to manage the social and psychological effects of the disease, the course of treatment, and the financial and logistical resources needed to maintain the course of treatment. "(B) Such screening described in subparagraph (A) shall occur within— "(i) the patient's first month of beginning the clinical trial, and "(ii) at pivotal points determined during the trial until the conclusion of the patient's participation in the clinical trial; "(C) The referral to an appropriate psychosocial support resource of any patient in the clinical trial who is identified based on the screening described in subparagraph (A) as having a high level of psychosocial distress in any or all of the enumerated psychosocial needs. "(D) All psychosocial distress measurements and referral determinations to the same level of detail as other laboratory tests or measurements taken to fulfill the objectives of the study.

"(b) MARKET EXCLUSIVITY.—A person who is found by the Secretary at the time of the filing of an application under section 355(b) of this title or section 262(a) of title 42 to have submitted the records described in subsection (a)(2) shall be entitled the following—

"(1) for an application pursuant to section 355 of this title for a drug, the 4- and 5-year periods described in subsections (c)(3)(E)(ii) and (j)(5)(F)(ii) of section 355, the 3-year periods described in clauses (iii) and (iv) of subsection (c)(3)(E) and clauses (iii) and (iv) of subsection (j)(5)(F) of section 355, and the 7-year period described in section 360cc of this title, as applicable, shall each be extended by 6 months; or

"(2) for an application pursuant to section 262 of title 42 for a biological product, the 12-year period described in subsection 262(k)(7)(A), the 4-year period described in subsection 262(k)(7)(B), and the 7-year period described in section 360cc of this title, as applicable, shall be extended by 6 months.

"(3) if the drug is the subject of—
"(A) a listed patent for which a certification has been submitted under subsection (b)(2)(A)(ii) or (j)(2)(A)(vii)(II) of section 355 of this title and for which psychosocial distress screening and referral records were submitted prior to the expiration of the patent (including any patent extensions); or
"(B) a listed patent for which a certification has been submitted under subsections (b)(2)(A)(iii) or (j)(2)(A)(vii)(III) of section 355 of this title, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

"(4) if the drug is the subject of a listed patent for which a certification has been submitted under subsection (b)(2)(A)(iv) or (j)(2)(A)(vii)(IV) of section 355 of this title, and in the patent infringement litigation resulting from the certification the court determines that the patent is valid and would be infringed, the period during which an application may not be approved under section 355(c)(3) of this title or section 355(j)(5)(B) of this title shall be extended by a period of six months after the date the patent expires (including any patent extensions).

"(c) GUIDANCE.—Not later than one year after the date of enactment of this section, the Secretary shall issue guidance on recommended psychosocial screening methods, referral plans and record keeping described in subsection (a)(2). "(d) DEFINITIONS.— "(1) PSYCHOSOCIAL DISTRESS.—For purposes of this section, the term "psychosocial distress" means a multifactorial, unpleasant, emotional experience of a psychological, social, or spiritual nature that may interfere with the ability to cope effectively with the patient's illness, its physical symptoms, and its treatment."

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Adler, N.E., Page, A.E.K. (2008). Cancer care for the whole patient: Meeting psychosocial health needs. Institute of Medicine (IOM). Washington, DC: The National Academies Press.

Andersen, B.L., Farrar, W.B., Golden-Kreutz, D.M., Glaser, R. et al. (2004). Psychological, behavioral, and immune changes following a psychological intervention: A clinical trial. *Journal of Clinical Oncology*, 22 (17), 3570-3580.

Case Western Reserve University
Response to Select Provisions of 21st Century Draft Discussion Paper

February 17, 2015

Title I

- Subtitle A – Patient-Focused Drug Development:
  - We are in favor of this provision - incorporating patient input on suggested benefits and risks of clinical trials is very important.
- Subtitle C – Approval of Breakthrough Therapies:
  - We are strongly in favor of this provision – increasing the use of a "breakthrough therapy" designation is a good policy.
- Subtitle J – Streamlined Data Review:
  - Attention should be given to the incorporation of a drug fact box on labels as has been previously suggested to the FDA.
- Subtitle K – Cures Acceleration Network:
  - We believe that the National Center for Advancing Translational Sciences (NCATS) should have the flexibility through use of Other Transaction Authority (OTA) funds. However, we are concerned that, barring other provisions, expanded efforts within NCATS outside the Clinical & Translational Science Awards (CTSA) programs may damage CTSAs. We need the national CTSA infrastructure to be robust for the Cures agenda to be sustainable. This is not currently addressed in the legislation.
  - Also, inter-institute cooperation is a key area that could accelerate therapies. Funds from the institutes should be brought together within NCATS if these initiatives are to be successful.
- Subtitle M – New Therapeutic Entities:
  - Incentivizing new therapeutic entities related to process/product improvements will extend patent life.

Title II

- Subtitle A – 21st Century Cures Consortium Act:
  - We are strongly in favor of the proposed Consortium.
- Subtitle L: NIH – Federal Data Sharing:
  - Data sharing is already mandated in NIH grants.
  - It is our concern that this additional provision may place more burdens on investigators who are already under significant administrative burdens.
- Subtitle M – Accessing, Sharing, and Using Health Data for Research Purposes:
  - Due to existing regulations, fulfilling this proposal would be challenging for researchers.
  - When data is used for research as opposed to commercial purposes, reducing fines and penalties for inadvertent record release would be a big help.
  - By making research a "safe harbor" for data, researchers will have an easier time accessing, sharing, and using health data – to the benefit of patients.

Title IV

- Subtitle A, Section 4001 – NIH Strategic Investment Plan:
    - We support a strategic plan within NIH, particularly one focused on inter-institute initiatives and burden reduction for researchers.
    - Streamlining the reporting and regulatory burdens is critical for national science productivity – these steps will enable more science to be done while operating safely and effectively.
    - Given this, we would encourage additional language to emphasize these initiatives.

- Subtitle I – Telemedicine:
    - There is no physical patient contact or examination with the process, so the issue should be well defined if a standard reimbursement is considered. As outlined, a physician would not be reimbursed if they called a patient on the phone to discuss their problem, but would if they happened to do so via Skype. As it is, it could be ripe for misuse and not achieve the good intentions of the concept.
    - Criteria for reimbursement for Telehealth Services should include: 1) documented medical necessity, 2) a provider licensed in the State, 3) have an established patient-physician relationship (will exclude new patients and consults), 4) proper documentation in medical records, 5) specific guidelines for reimbursement (complexity vs. time-based vs. flat fee) and 6) security measures that are in place.
    - It is essential that there is a related language regarding Telehealth Monitoring, as both issues will be germane for value-based reimbursement.

For more information, contact:
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February 10, 2015

Re: Refinements to 21st Century Cures to Ensure Americans Have Access to New Antibiotics in the Community Setting to Treat Drug-Resistant Bacteria

Dear Chairman Upton and Congresswoman DeGette:

I am writing on behalf of Cempra Pharmaceuticals and the patients we serve to thank you for the opportunity to comment on the initial draft of the 21st Century Cures legislation. Our comments focus on the bipartisan effort to ensure that all Americans have access to effective antibiotics that address the growing crisis involving drug-resistant bacteria. We commend the authors for including provisions to help protect patient access to new antibiotics in the inpatient hospital setting. As a small but critically important refinement, we urge you to include legislative language to protect patient access under Medicare to new oral antibiotics in the community (outpatient) setting.

Cempra Pharmaceuticals of Chapel Hill, NC was founded in 2006 to meet the need for new antibiotics for treating drug resistant pathogens. Cempra is developing and manufacturing these products within the United States. For example, Cempra developed Solithromycin, a novel antibiotic currently undergoing Phase III trials that holds the promise for treating resistant strains and maintaining effectiveness against resistance in the future. Solithromycin is being developed as oral capsules, pediatric oral suspension and intravenous formulations and has distinct advantages over the current standard of care, including activity against existing drug resistant strains.

The Problem of Antibiotic Resistance to Oral Drugs for Use in Community Settings

We are facing an emerging health care crisis as our existing arsenal of antibiotics to treat common community-acquired infections is not keeping pace with the rapid emergence of drug resistant strains of bacteria. Thousands of people are already dying each year in the United States as a direct result of drug resistant infections acquired in their communities. In addition to the resulting mortality and human suffering, the growing presence of drug resistant bacteria is having significant adverse impacts on our health care system and our economy. As one example of this overarching problem, the number of hospital discharges and the escalating costs of hospital readmissions for community-acquired pneumonia (CAP) caused by drug resistant bacteria is steadily rising each year. CAP is one of the most common infectious diseases caused by strains of bacteria that are resistant to traditional antibiotics and CAP is a significant cause of mortality and morbidity throughout the United States.

There continues to be inadequate development of new antibiotics. Although some new IV antibiotic products are under development for use in the hospital inpatient setting, there is an even more dramatic shortage of oral antibiotics under development that can be readily used in the future in the outpatient community setting. The need for new oral antibiotics for use in the community setting is acute, and the most effective way to attract more investment in novel antibiotics is to establish federal policies that ensure patients will have access to these drugs in the outpatient setting in the future.

Solution: Protect Patient Access to Certain Novel Antibiotics in the Community Setting

We urge Congress to enact explicit patient safeguards to protect clinically appropriate access to new antibiotics in the community-based setting. The proposed provision will protect patient access under Medicare for new antibiotics that address the increasing threat arising from antibiotic resistance. The rates of community-acquired infections that are resistant to traditional antibiotics are rising at alarming rates, and this provision will ensure that Medicare beneficiaries who rely on the Medicare Part D prescription drug benefit will have access to new oral antibiotics developed for use in their own homes rather than in the hospital or other institutions. The scope of the protection is targeted to apply only to antibiotics that meet criteria related to antibiotic resistance based on determinations by both the Food and Drug Administration (FDA) and the Centers for Disease Control and Prevention (CDC).

In particular, Part D prescription drug plans would be required to cover drugs that are designated as qualified infectious disease products (QIDPs) by the Food and Drug Administration (FDA). QIDPs are antibiotics or antifungals that are intended to treat "serious or life-threatening" infections that are caused by drug resistant pathogens, emerging pathogens, or qualifying pathogens that have been identified by the Secretary. The antibiotic must also be indicated for the treatment of pathogens that the CDC has identified as posing urgent or serious threats due to antibiotic resistance. The provision further protects patient access by capping patient cost-sharing under Medicare Part D at a $20 co-payment or 10% coinsurance rate after the enrollee has met their deductible.

Proposed legislative language follows below:

(a) Section 1860D-4(b)(3) of the Social Security Act is amended by inserting after subparagraph (H) the following new subparagraph—

"(I) DRUGS ADDRESSING THE THREAT OF ANTIBIOTIC RESISTANCE.—The Secretary shall ensure that formularies include all covered Part D drugs that are designated by the Food and Drug Administration as Qualified Infectious Disease Products for the treatment of serious or life-threatening infections under section 505E of the Federal Food, Drug, and Cosmetic Act and are approved by the Food and Drug Administration after December 31, 2014 for indications caused by pathogens that the Centers for Disease Control and Prevention identified as causing an urgent or serious threat level due to antibiotic resistance prior to the date of approval. After a Part D eligible individual has incurred costs equal to the annual deductible, the cost-sharing incurred by a Part D eligible individual for drugs described in this subparagraph shall not exceed the greater of a copayment of $20 or coinsurance of 10 percent.

* * * *

Thank you for your attention to this important issue. We would be pleased to provide additional information. Please do not hesitate to contact David Moore, Chief Commercial Officer at Cempra at dmoore@cempra.com or Julie Shroyer, Senior Policy Advisor at Polsinelli at jshroyer@polsinelli.com with any questions.

CLEAR CHOICES
A MOVEMENT FOR INFORMED HEALTH CARE

February 19, 2015

Congressman Fred Upton
Chairman, Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton and Ranking Member Pallone,

The Clear Choices Campaign is pleased to submit comments on the 21st Century Cures Initiative. Clear Choices is a consumer-industry coalition dedicated to making health markets more transparent, accountable and consumer-friendly. Clear Choices is committed to ensuring patients have as much access to information as possible, so they can make informed plan selections and have adequate access to the healthcare system. We believe doing so will not only empower consumers, it will improve quality, improve health outcomes and lower health costs. Realizing this potential will require the broader availability and use of information and data to generate meaningful and accurate comparative information on health plan and provider choices.

Our thoughts on the draft legislation are outlined below. The suggestions provided in this letter reflect the Coalition's, and not necessarily those of any of our individual members.

Subtitle F – Building a 21st Century Data Sharing Framework

We support the inclusion of changes to the CMS Data Sharing Program in the discussion draft. This much-needed legislation would expand the scope and uses of data under the Qualified Entity (QE) program and establish strict procedures to ensure that the data remains secure and patient information is protected. We believe that expanding the availability of Medicare claims data will provide valuable insights into the quality, value and outcomes of medical care. These insights can lead to a range of beneficial outcomes, including allowing consumers access to better comparison-shopping tools, to helping providers pursue quality improvement and patient safety initiatives and enabling payers and providers to work together to build higher-performing networks. Analyses based on data can yield insights with respect to practice patterns that, in turn, will allow consumers and health plans to make better-informed choices while providing timely feedback to providers. Ultimately, this data will help power tools, like web sites and apps that will provide information to promote more informed consumers.

Unfortunately, the existing QE statute is ill-suited to these purposes. QEs may only use subsets of claims data for the limited purpose of publishing aggregate, non-provider-specific analyses. The discussion draft addresses this deficiency by permitting non-public uses of data by responsible commercial and nonprofit entities. We believe the language in the bill can be improved and offer the following suggestions:

1. **Expand the Number of Downstream Users.** The discussion draft expands the types of entities that may access data or analysis to include providers, suppliers, medical societies and

hospital organizations, employers and insurers. Because program rules and the bill envisions prohibitions on re-disclosures or inappropriate uses subject to penalties, we encourage you to broaden the list of downstream users to include other stakeholders such as:

a. Health data analytics companies
b. Public health authorities,
c. state and local government agencies
d. health plans

These entities either have a need that can be filled via use of the data (public health improvement, population health management) or special expertise that can bolster the use of data (research findings, disease management, etc.).

2. **Expand the Uses of Data.** The discussion draft limits the allowable uses of data to assisting providers in quality improvement and new models, patient care improvement activities, population health management, disease monitoring and for combination with qualified clinical registries. We encourage you to also add efficiency, cost containment and fraud prevention and reduction activities to the list of allowable uses, because it will help foster better care outcomes at lower costs.

3. **Permit QEs to provide or resell de-identified Medicare data to employers and health plans**. The bill explicitly bars QEs from reselling combined Medicare and commercial claims data to self-insured employers and insurers, who operate health plans. We share the concern, voiced by antitrust experts, that the resale of proprietary claims data could run afoul of policies that forbid health plans from sharing proprietary pricing information. However, we believe this concern is best addressed through limits on the resale of commercial, not Medicare, data. Health plans would, as a matter of course, combine Medicare claims data with proprietary data—thereby limiting the utility of having QEs combine the data beforehand. In fact, a health plan might be less likely to share its proprietary claims data with a QE if it believed the data would be resold to competitors. To complement this greater access, we strongly support the bills' requirement that recipients of the data ("subscribers") be contractually bound, through enforceable Data Use Agreements, not to re-identify the data.

4. **Streamline the review and correction process for non-public analyses by replacing the obligation of QEs to notify and solicit corrections from providers identified in such analyses with the qualified right of a provider to request such reviews.** The reforms carry over to non-public analyses a QE's current obligation to assure the accuracy of published reports by giving named providers the right to correct any errors prior to publication and in each instance. We are concerned that each internal analysis using Medicare claims data might trigger an obligation to notify and share proprietary information with providers, the effect of which could be to discourage the intended uses of Medicare data. Indeed, if every update of public or private data triggers a new round of notifications, providers themselves could be overwhelmed. We agree that providers need a process for correcting errors but suggest this be done once at the data level. For non-public analyses, we suggest allowing providers to review the methodologies of non-public analyses upon request, where they have reason to believe that such analyses are materially harming their businesses.

5. **Subscribers of QEs who violate Data Use Agreements, through unauthorized disclosures or the re-identification of patient data, should be barred from future access to Medicare claims data.** We support the legislation's civil penalties for breaches of data security, but also urge the Committees to clarify that: (1) CMS should bar meaningful violators from the future receipt of such data; and (2) QEs have an affirmative duty to promptly report any breaches to CMS.

We believe the reforms in the discussion draft are an essential step toward creating a consumer friendly, customer-centered health system.

Section 4221 Medicare Site-of-Service Price Transparency

We strongly support the provision to establish and update a searchable public database to disclose to Medicare eligible individuals information on costs for each payment area by zip code and item or service. The information would include a list of items and services by site of care, a list of providers within the area and whether they are in network, the maximum out-of-pocket cost, including deductible and cost sharing and the rate of payment without regard to cost sharing. We suggest clarifying the information is available to the public at large, and not just Medicare beneficiaries. Clear Choices believes the information provided by this section will allow consumers to be better informed prior to selecting sites of care at which they receive services.

Conclusion

We appreciate the opportunity to share our initial thoughts with you on these issues and your dedication and commitment to ensuring the discovery, development, and delivery of innovative health care products and services. We look forward to working with you as you pursue the 21st Century Cures initiative.

Sincerely,

[redacted]

Joel C. White
President

February 10, 2015

The Honorable Fred Upton
Chairman
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Re: Comments regarding the 21st Century Cures Discussion Draft

Dear Chairman Upton:

The CME Coalition supports the manifest goals of the Energy and Commerce Committee's *21st Century Cures Initiative*, and endorses the Committee's efforts to streamline the implementation of new medical treatments. Further, we understand that unless doctors are given the tools and education they need to implement the newest innovations in medicine, the promise of 21st Century Cures won't make it to the bedside – and so, we applaud the Committee for including an important provision in the discussion draft to ensure that access to continuing medical education (CME) will not be an unintended casualty of unnecessary regulation.

Specifically, the Coalition welcomes the inclusion of a measure—based on legislation (H.R. 293) introduced by Reps. Michael Burgess (R-TX) and Peter DeFazio (D-OR)—which would appropriately exempt CME and certain educational materials from the reporting requirements of the Physician Payment Sunshine Act. While the Sunshine Act intended to make payments to physicians more transparent, the Centers for Medicare and Medicaid Services' (CMS) has ostensibly defied Congressional intent, providing a smattering of regulatory interpretations that have called into question whether continuing medical education events could be subject to the law's reporting requirements, making them less accessible to physicians. The bipartisan provision included in the Committee's discussion draft (Section 4381) was authored in response to these unintended consequences, and would ensure that physicians will have access to the innovations in medicine that the 21st Century Cures initiative is intended to stimulate.

The CME Coalition recognizes the importance of ensuring that physicians are encouraged to continue in their professional development, and looks forward to working with the Committee in fulfilling that mission. Further, the Coalition would welcome the opportunity to present

suggestions that would ensure that the legislative language included in the bill avoid any ambiguity that could raise future questions about the reporting requirements for CME events.

About the CME Coalition

The CME Coalition represents a collection of continuing medical education provider companies, in addition to other supporters of CME and the vital role it plays in our health care system. Our member organizations manage and support development of healthcare continuing education programs that impact more than 500,000 physicians, nurses and pharmacists annually.

Graduation from medical school and completion of residency training are the first steps in a career-long educational process for physicians. To take advantage of the growing array of diagnostic and treatment options, physicians must continually update their technical knowledge and practice skills. CME is a mainstay for such learning. Most State licensing authorities require physicians to complete a certain number of hours of accredited CME within prescribed timeframes to maintain their medical licenses. Hospitals and other institutions may impose additional CME requirements upon physicians who practice at their facilities.

More than 400,000 medical journal articles are published each year, making the practice of medicine very dynamic. The sheer volume of new scientific data and changes in medicine requires as many appropriate avenues for funding certified CME as possible. In addition, the changes to practice in medicine occur rapidly. The nature of medicine involves constant advancement, testing, and application. Medicine features landmark breakthroughs, such as the discovery and testing of a new therapeutic agent.

Changes in medicine often are revolutionary. Patients and society demand that our physicians receive information instantaneously, and that updates in treatment, diagnosis, and prevention are disseminated to physicians as soon as practically possible. Without CME, health care practitioners cannot get the most recent and up-to-date advances. Such advances are pivotal in allowing physicians to begin implementing

Background on the Sunshine Act

The Physician Payment Sunshine Act is a healthcare policy first introduced in 2007 by Senators Charles Grassley (R-IA) and Herb Kohl (D-WI), which was later incorporated into law as a part of the Affordable Care Act, passed in March 2010. A measure intended to bring transparency to financial relationships between providers and industry, the Sunshine Act requires pharmaceutical and device manufacturers to report their direct and indirect payments or other transfers of value made to healthcare providers and teaching hospitals (covered recipients). This financial data is collected by the Centers for Medicare and Medicaid Services (CMS), who report the information publicly on a website launched in September 30, 2014.

While the Sunshine Act was designed to shed "light" on potential conflicts of interest, it was never the intent of Congress to expand the public reporting requirements to include transactions related to the provision of continuing medical education when such payments are made from commercial interests to CME providers without allowing for the supporting entity to enjoy any control regarding either the presenters, the curriculum, or the attendees of a given educational program. Specifically, the Sunshine Act protected CME by excluding coverage of indirect payments to "covered recipients" by "applicable manufacturers," such as industry contributions to CME programs.

Unexpectedly, in a December 2011 proposed rule, CMS indicated that they would rely on a "catch-all" provision in the Sunshine Act to require reporting for most CME providers, professional medical associations, patient advocacy groups, and other non-profit organizations. While CMS never finalized this proposal, the agency has advanced a variety of different rules around reporting for CME that has confounded stakeholders left CME providers with many questions about what information they are required to collect. Indeed, the Wall Street Journal recently reported that the most recent guidance from the agency "marks the fifth time that CMS has offered yet another interpretation of its final rule on disclosing CME payments."

As CMS struggles with their implementation of the Sunshine Act, CME stakeholders face an environment clouded with uncertainty as they seek to secure commercial support for future curricula. And with the current rule on CME payment disclosures scheduled to take effect in 2016, there is a limited window of time to act before speakers and attendees will be directly impacted by CMS' indecision in the rulemaking process.

How CME Improves Patient Outcomes

In order to appreciate the rationale for exempting CME-related payments from Sunshine Act reporting, it is necessary to have an appreciation for the intrinsic value of CME and the role it plays in our healthcare system. Graduation from medical school and completion of residency training are the first steps in a career-long educational process for physicians. To take advantage of the growing array of diagnostic and treatment options, physicians must continually update their technical knowledge and practice skills. CME is a mainstay for such learning. Most state licensing authorities require physicians to complete a certain number of hours of accredited CME within prescribed timeframes to maintain their medical licenses.

Several studies in the past few years have analyzed the impact of continuing medical education on improving patient care. The studies have repeatedly shown that physicians who are educated about the latest advances in evidence-based practice will make more informed treatment decisions, resulting in improved patient outcomes. Some examples of recent studies include an industry-supported CME program for multiple sclerosis, which demonstrated "statistically significant changes in participant knowledge and competence across a broad range of patient-care topics."[1]

[1] *Multiple Sclerosis CME/CE Live Intervention Demonstrates Improved Clinician Knowledge*, published by Med-IQ October 2, 2012

Another study found that physicians who attended an industry-supported educational activity for chronic obstructive pulmonary disease were 50 percent more likely to provide evidence-based care than nonparticipants were.[2] In addition, patients suffering from hypertension were 52 percent more likely to receive evidence-based hypertension care when they were seen by physicians who attended an industry-supported educational activity than those seen by nonparticipants.[3] Yet another study showed that "heart disease patients whose general practitioners participated in an interactive, case-based CME program had a significantly reduced risk of death over 10 years compared with those whose doctors didn't receive the education."

In recent years, commercial funding for CME has dropped significantly, yet little has been written about how this might affect CME in fields such as oncology, where new drugs and advances emerge at a rapid pace. Commercial support represented 25.9 percent of total CME funding in 2013, down from 46 percent of total funding in 2007.[4]

The *Journal of Cancer Education* published a study in April 2014 that surveyed close to 300 oncologists about the role of industry-supported CME in their professional development and patient care.[5] The study found that 90 percent of oncologists "agree" or "strongly agree" that commercial support may be more necessary for oncology than for other specialties due to the rate at which cancer therapies are introduced. Respondents indicated that commercial support plays an important role in providing this cutting-edge information. Three-quarters of the oncologists indicated that commercial support is a significant reason high-quality oncology CME is available. Furthermore, approximately 88 percent said it is "somewhat" to "very likely" that implementation of new or emerging therapies would be slower if commercial support is reduced, and 89 percent said implementation of evidence-based medicine would be slower. When asked about their concerns with removing commercial support, oncologists responded that the lack of commercial support for CME would negatively impact the cost of CME, the availability of professional development opportunities, and access to CME.

In summary, the creation of new products will produce enduring social gains only if physicians are properly trained and educated about these advances. Pharmaceutical companies invest billions of dollars in creating new treatments for patients every year. Patients count on doctors to be up to date with these latest medical breakthroughs, and CME provides doctors with that knowledge.

Why the Sunshine Act Exemption Matters for CME

As strong advocates for CME, we see the education of medical practitioners as an indispensable ingredient in the expansion of health care innovations and improvements in patient outcomes. A

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[2] *Improving COPD Patient Outcomes: Breaking Down the Barriers to Optimal Care*. American College of Chest Physicians annual meeting Chest 2010 in Vancouver, British Columbia.

[3] Drexel, C. et al. *J Clin Hypertens* (Greenwich). 2011 Feb;13(2):97-105

[4] ACCME 2013 Annual Report

[5] Robinson, C et al. *The Consequences of Diminishing Industry Support on the Independent Education Landscape: An Evidence-Based Analysis of the Perceived and Realistic Impact on Professional Development and Patient Care Among Oncologists*, J Cancer Educ. 2014.

robust commitment to CME requires adequate resources from across the healthcare system. It also requires the participation from expert practitioners and academics who are willing to take the time to share their knowledge with other medical professionals.

We harbor great concern that a requirement for CME-related payments to be reported will cause many leaders in their field to forego participation in CME rather than have to answer questions related to the so-called commercial payments they were reported to have received. Indeed, in a recent poll of 527 CME participants, almost 70 percent stated that the elimination of the CME exemption would discourage them from participating in industry-supported CME activities.[6]

Conclusion

We are passionate about continuing medical education because we see the direct beneficial impact it has on physician excellence and patient outcomes. Forcing indirect and independent "transfers of value" to providers who participate in and speak at these events to be reported in the Sunshine Act database will have an unmistakable and chilling effect on physician, and commercial supporter, participation in CME. Any benefit that might be gained from requiring the publication of these "payments" in the form of subsidized tuition or faculty speaking fees is simply not equaled by the predictable, negative impact on this vital component of our healthcare system.

The Energy and Commerce Committee's *21st Century Cures Initiative* has the potential to transform the way that advancements in medicine are discovered and developed. But unless doctors are able to access these latest updates in medical innovation through continuing education, and without fear of the stigma that comes with being "reported" in a CMS database, we risk falling short on our promise to deliver the latest science to our patients' bedsides. We look forward to working with the Committee to ensure the preservation of CME as a valuable pillar of our healthcare system, and would welcome the opportunity to work with the Committee to ensure that legislative language adequately protects CME.

Sincerely,

Andrew M. Rosenberg, J.D.
Senior Advisor, CME Coalition

Cc: The Honorable Frank Pallone, Ranking Member, Energy & Commerce Committee
The Honorable Diana DeGette

[6] *2014 Opinions about Elimination of the CME Exemption on the Sunshine Act*, Primary Care Network, Aug. 14, 2014

February 3, 2015

The Honorable Fred Upton
2183 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton:

As you work to introduce and pass the 21st Century Cures legislation, the undersigned organizations urge you to address medication access and affordability issues by including the Patients' Access to Treatment Act (PATA) in the final bill. We applaud your effort to improve the discovery, development and delivery of medical treatments and cures. Based on the roundtables and hearings the Committee has held over the last eight months on the 21st Century Cures Initiative, we know you are well aware that if patients cannot access these treatments and cures, the discovery and development you seek to foster and accelerate will not deliver the benefits to the very people they are intended to help.

Your draft legislation goes a long way towards including patients in the bio-medical research process and addressing issues around chronic disease, such as creating a framework at FDA to better incorporate patient experiences in the drug development process, and authorizing a longitudinal study to improve the outcomes of people with chronic diseases. We believe inclusion of PATA will help address access and affordability of medications, and satisfy this important pillar of the research continuum.

Accessing affordable medications is vital for those with such chronic, disabling and often life-threatening conditions as multiple sclerosis, rheumatoid arthritis, psoriatic arthritis, lupus, cancer, HIV, and primary immunodeficiency diseases. Studies show that the higher the out-of-pocket costs, the less likely patients are to take their medications on time, if at all. Foregoing medications often results in disability and other health complications that can lead to poor long-term health outcomes and increase health costs.

Breakthroughs in new medications such as biologic drugs are helping people with chronic diseases lead productive lives. These medicines, while revolutionary, are complex to manufacture and distribute, and are often very expensive. The cost of specialty medications like biologics has pushed health insurers to use enhanced benefit design to balance access and cost. An alarming trend in today's health insurance market is the practice of moving vital medications like biologics into specialty tiers that utilize high patient cost-sharing methods. Specialty tiers commonly require patients to pay a percentage of the cost of the drug or a co-insurance that can range from 25% to 50%, costing the patients hundreds of dollars, even thousands of dollars, per month out of pocket for a single medication.

PATA, soon to be re-introduced by Representatives David McKinley (R-WV) and Lois Capps (D-CA), proposes to limit cost-sharing requirements applicable to medications in a specialty drug tier (typically Tier IV or higher) to the dollar amount applicable to drugs in a non-preferred brand drug tier (typically Tier III). This bill would greatly increase access and affordability of specialty medications, thereby reducing disability and constraining health care costs over time.

This bi-partisan legislation had over 140 co-sponsors in the last Congress, and enjoys wide support among patient and provider advocacy groups. Including PATA would not only satisfy access and affordability, but also complement many of the provisions under Title IV of the draft legislation,

particularly Rep. Gus Bilirakis's provision allowing Medicare beneficiaries to better identify the out-of pocket costs given their treatment.

Patients need access to the cures and treatments the 21st Century Cures Initiative is intended to advance. Legislation modernizing the bio-medical research enterprise must address access and affordability issues to benefit the very people this research is intended to help. Again, we urge you to include PATA in the final 21st Century Cures legislation and we look forward to working with you to bring better treatments – and ultimately cures – to patients. Please contact Anna Hyde at the Arthritis Foundation at ahyde@arthritis.org or 202-887-2917 with any questions.

Sincerely,

American Academy of Dermatology Association
American Academy of Neurology
American Autoimmune Related Diseases Association
American College of Rheumatology
American Society of Hematology
Arthritis Foundation
Colon Cancer Alliance
Crohn's and Colitis Foundation of America
Digestive Disease National Coalition
GBS/CIDP Foundation International
Hepatitis Foundation International
Hemophilia Federation of America
Hematology/Oncology Pharmacy Association
Immune Deficiency Foundation
International Foundation for Functional Gastrointestinal Diseases
Leukemia & Lymphoma Society
Lupus Foundation of America
National Brain Tumor Society
National Hemophilia Foundation
National Organization for Rare Disorders
National Psoriasis Foundation
Patient Services Incorporated
Pulmonary Hypertension Association
Scleroderma Foundation
Sjogren's Syndrome Foundation
Sleep Research Society
Spondylitis Association of America
The AIDS Institute
US Hereditary Angioedema Association

February 10, 2015

The Honorable Fred Upton
Chairman
Committee on Energy & Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton:

On behalf of the Coalition for Pediatric Medical Research, a collaboration of our nation's top children's hospitals, and FightSMA, a leading organization working to create treatments and a cure for spinal muscular atrophy, we are writing to thank you for including within your 21st Century Cures discussion draft Sec. 3041 to improve the National Pediatric Research Network Act (Title II of Public Law 113-55).

As you are well aware, the National Pediatric Research Network Act has enjoyed overwhelming Congressional support leading up to its enactment in late 2013. Unfortunately, despite this backing, the National Institutes of Health (NIH) has not moved forward in a material way to implement the law over the past year-plus. The provision included in the Cures discussion draft will help overcome these impediments by making a few targeted amendments to the law. Specifically, the proposed changes would:

- Prevent NIH from implementing the law simply by making modest changes to existing networks and other projects. While we welcome applying reforms of the law more broadly to enhance other NIH-funded initiatives, we are concerned that doing so without implementing the core network law would not achieve the intent of the law.

- Clarify that the Office of the Director can work with any other research institutes and centers to implement the NPRNA.

- Direct the NIH to implement the law in a timely, substantive and meaningful manner.

As you and your colleagues work to advance this discussion draft and move 21st Century Cures forward, we urge that you ensure this provision is included throughout the process, and we look forward to supporting your efforts in this regard.

If you have any questions or would like additional support from the Coalition or FightSMA, please contact Nick Manetto at 202.312.7499 or nicholas.manetto@faegrebd.com, or Steve Eichenauer at 202-783-2596 or seichenauer@psw-inc.com.

Sincerely,

Nick Manetto
For the Coalition for Pediatric Medical Research

Steve Eichenauer
For FightSMA

CHPA CONSUMER HEALTHCARE PRODUCTS ASSOCIATION
founded 1881

February 5, 2015

The Honorable Fred Upton
Chairman, House Energy & Commerce Comm.
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Diana DeGette
House Energy & Commerce Committee
U.S. House of Representatives
2368 Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Upton and Congresswoman DeGette:

We noted with interest the House Energy & Commerce Committee's release of a discussion draft for the 21st Century Cures initiative. We applaud the effort that went into the draft and your goal to address how we can accelerate discovery, development, and delivery of new treatments and cures for patients.

The Consumer Healthcare Products Association (CHPA) is the 134-year-old trade association representing the leading manufacturers and marketers of over-the-counter (OTC) medicines and dietary supplements. Every dollar spent by consumers on OTC medicines saves the U.S. healthcare system $6-7, contributing a total of $102 billion in savings each year. CHPA is committed to promoting the increasingly vital role of over-the-counter medicines and dietary supplements in America's healthcare system through science, education, and advocacy.

Many of our member companies market OTC medicines under new drug applications (NDAs). As such, we have an interest in a number of provisions in the discussion draft which would apply to OTC NDAs or studies just as they apply to prescription NDAs or studies. While we understand this is a discussion draft, and we may want to suggest specific changes to language as a bill moves forward, broadly speaking, several provisions in the discussion draft could enhance the environment for the switch or transfer of prescription medicines to OTC status when proven safe and effective under a sponsor's NDA. Among these provisions are:

- ***Section 1001, patient-focused drug development***: The discussion draft would require FDA "to establish a structured framework for the meaningful incorporation of patient experience data into the regulatory decision-making process." Implementing a more structured risk-benefit framework is something FDA has already begun to undertake and has influenced OTC NDA sponsor thinking on how to approach switch applications. This section would only accelerate that movement. We also applaud the effort require FDA to provide more structure through guidance for patient-reported outcomes, including in clinical trials and drug submissions.

- ***Section 1161, modernizing the regulation of social media:*** This provision would be useful in expanding the manner in which sponsors communicate truthful information to consumers, and add clarity and transparency to how FDA views social media.

- ***Section 1241, new therapeutic entities:*** This section's extension of "up to 2 years" beyond the existing 3 years of exclusivity for NDAs or supplemental NDAs with essential clinicals for new indications; or new delivery systems or formulations that promote greater patient adherence, reduce the manner or extent of side effects, or provide other comparable benefits would encourage investment for new indications or better formulations, ultimately to the benefit of consumers.

- ***Sections 2016-2063, sensible oversight for technology which advances regulatory efficiency:*** While there are many specifics to sort through, the concepts of this section could be useful in both prescription-to-OTC switch support programs and in gathering patient-reported outcomes.

- ***Section 2101, utilizing real-word evidence***: This concept of requiring FDA guidance for standards, methods, and circumstances through which NDA sponsors could submit data about the usage, benefits, or risks of a drug from sources other than randomized clinical trials, including observational studies, registries, or patient reported outcomes could be very helpful in expanding the sources of data to demonstrate safe use and the benefits of new medicines.

- ***Section 2141-2, combination products:*** Clarifying FDA's internal procedures, single point accountability, and the conduct of meetings for drug-device combination products would add useful transparency and predictability for the makers of these products.

- ***Section 2181, interoperability***: Today, electronic medical records to not have a means to capture OTC medicine utilization. Looking ahead, it would be useful to have that capacity in these systems, since it will be one means to generate data on the cost effectiveness of these medicines.

- ***Section 3031, post-approval studies and clinical trials:*** A number of prescription-to-OTC switch NDAs have included post-approval commitments. It would therefore be useful to have a means to address whether those commitments are still relevant.

As we continue to gather information on company views around these and other provisions, we hope to have the opportunity to suggest potential refinements or changes. For instance, similar to section 2101 on utilizing real-world evidence, the concept of the device provision on valid scientific evidence (section 5062) could bring clarity to the value of peer-reviewed literature in drug applications.

We look forward to working with Members of Congress as this process moves forward.

Very Truly Yours,

[redacted]

Scott M. Melville
President and CEO
Consumer Healthcare Products Association

The Honorable Fred Upton and Diane DeGette
February 5, 2015

CC:
The Honorable Frank Pallone
The Honorable Joe Pitts
The Honorable Gene Green

21CC-comment-Feb2015

Comments from Martha Brumfield, Critical Path Institute

First Draft 21st Century Cures

My overall impression is that there are some elements in this proposed bill which can be helpful if implemented judiciously. However, an overriding concern is the huge administrative burden being placed on FDA to hold public meetings, generate draft guidance documents and meet other prescribed deadlines at a time when they are already sorely under resourced to meet their current obligations. Since FDASIA was signed, FDA has not been able to staff to the level needed today. Simply adding more resource on paper will not solve anything. FDA needs to be able to expeditiously move through the government hiring process and to recruit talent with the expertise required.

BIOMARKERS

Specific to the biomarker components, FDA has already implemented a process for much of what is proposed in this draft bill. What FDA really needs are the resources to conduct their reviews in a timely manner. For example, FDA has a very logical process in place for biomarker qualification. The process works but would benefit from defined timelines for FDA review and comment for each step in the process. The process as of today includes: the Letter of Intent (which defines the need for the new biomarker, the context of use that will be pursued by the sponsor and a general concept of the research plan), the Briefing Document (which includes the details of the research plan and the evidence that the sponsor intends to ultimately submit in support of a regulatory decision); and the final submission (which includes the raw data and evidence to support the Context of Use as agreed with FDA resulting from the Briefing Document).

Some of the timelines for FDA review (e.g., 90 days for FDA to make a decision on a biomarker) included in the current draft are not reasonable. My recommendation would be the following:

Letter of Intent	FDA response within 30 days
Briefing Document	FDA response and meeting scheduled within 90 days
Final Submission	FDA response and decision within 180 days

Setting up the qualification process to follow closely CDER's current process for review of INDs, NDA, BLAs is the most logical way to proceed.

Legislation could address one of the major obstacles for qualifying biomarkers, which is the inability to access and analyze biomarker data. If a safe harbor was established for the extensive biomarker data that is submitted to the FDA as part of INDs, NDA and BLAs, biomarkers could be rigorously vetted and validated. Such an activity would optimally be carried out by a neutral third party with the requisite subject matter expertise.

An element that is most needed but which cannot be legislated is for the scientific community to embrace the need for more rigor and standardization in data collection and greater collaboration in helping to define the evidentiary standards that are appropriate for different types of biomarkers. FDA could coordinate meetings to encourage this discussion or could request that a neutral, third party undertake the coordination of these meetings. However, the scientific community at large must be willing to embrace a culture change towards a collaborative, team science approach if we are to shift the paradigm.

21st Century Cures Consortium

It is my belief that a better approach is to authorize and resource FDA to fully implement the elements of the Critical Path Initiative. The opportunities which were clearly defined in FDA's 2004 and 2006 publications have not been fully met and have the potential to expedite decision making along the drug development process. FDA and industry scientists are best positioned to understand where science should advance in the drug development and regulatory decision making pathway. If Congress is committed to establishing a broader consortium then I strongly recommend the adoption of key elements of the IMI model. First and foremost, to ensure a focus on drug development, industry representatives (Heads of R&D) should constitute at least 50% of the governing board and FDA should have multiple representatives (CDER, CBER, CDRH, and the Office of the Commissioner). Furthermore, the requirements for award of grants or contracts should mandate: (1) meaningful collaboration within the consortium and with outside efforts to prevent duplication of effort and to best utilize limited resource, (2) data sharing, (3) use of regulatory required data standards, (4) focused deliverables against timelines, (5) transparency and public access to deliverables. The Cures Consortium should be led by a neutral organization with deep experience in bringing together diverse stakeholders to develop and execute research plans focused on drug development.

I fully support elements which encourage FDA and EMA to continue and even increase their collaboration. I would propose also that if the 21st Century Cures Consortium goes forward, that it be mandated to closely collaborate with IMI.

CUREalliance for mental illness

Educate. Advocate. Cure.

470 Lloyd Avenue
Providence, RI 02906

401.369.4017

www.curealliance.org

February 16, 2015

The Honorable Fred Upton, Chair
The Honorable Diana DeGette, Member
House Energy and Commerce Committee House Energy and Commerce
2125 Rayburn House Office Building Committee
Washington, DC 20515

Sent via e-mail: cures@mail.house.gov

Dear Chairman Upton and Representative DeGette,

We would like to respond to the recently released discussion draft of the 21st Century Cures Act.

Cure Alliance for Mental Illness is an organization advocating for increased research in mental illness and providing information and education on the science of mental illnesses.

We are grateful for the work of the Energy and Commerce Committee and all the members of Congress for their hard work on the 21st Century Cures Act. We support the Act's goal of accelerating the discovery, development, and delivery of treatments and cures, as new and improved cures are a desperate need in the area of mental illness.

As members of the American Brain Coalition, we would like to endorse its letter of response to the draft legislation of the Act, and would like to mention specifically certain points raised in ABC's response.

1. We strongly support ABC's call for increased biomedical research funding. The budget of the NIH has been decreasing in real dollars for over a decade, which has negative consequences for patients, for researchers and related industries, and for our nation's position at the forefront of biomedical research globally. In particular, we support increasing the funding for the BRAIN Initiative, as the Act proposes, and urge that this initiative be funded generously. While neurological and psychiatric diseases together carry the largest disease burden (more than cardiovascular disease), our understanding of the brain is still in its infancy.

2. We share the ABC's caution about the proposed 15-year period for market exclusivity for specialty drugs. While we understand the cost barriers to bringing drugs to market, given long development times, we feel it is extremely important to find ways to balance this against the needs of patients. For psychiatric patients, prescribed medications can be cripplingly expensive but essential to living a productive life.

3. We support the proposals for strengthening the effectiveness of the FDA, and note the importance of that agency in protecting patients and promoting the safety of the American public. We agree with ABC that the FDA must have adequate funding to succeed in the enormous amount of oversight it is tasked with.

4. With ABC, we are concerned about any language that limits the scientific independence of the NIH. It is certainly appropriate—indeed critical—that our elected representatives direct the focus of the National Institutes of Health to the health issues that affect us most. In this we urge Congress to give the most weight to the recent US Burden of Disease study, which points out the massive cost of brain disorders to our people. However, the details of how the work should be done requires a process that is not unduly influenced by political pressures, and we support ABCs recommendation against adopting provisions that would infringe on the peer-review system of scientific funding.

5. Regarding SEC. 4021. NATIONAL NEUROLOGICAL DISEASES SURVEILLANCE SYSTEM: With the ABC, we support the idea that the Centers for Disease Control and Prevention assess and inform the nation about the epidemiology of brain and other nervous system disorders. However, we do not support limiting this system to Parkinson's disease or multiple sclerosis. We should have good data on the true incidence and prevalence of all nervous systems disorders—from Alzheimer's and bipolar disorder to schizophrenia and post-traumatic stress disorder.

Again, thank you for your work on this important initiative. We have the potential in the U.S. to advance biomedical knowledge and treatments to benefit not only ourselves but the entire world. To realize this potential, we need this kind of careful attention to improving the systems that support biomedical innovation. Please feel free to contact me at hakon.heimer@curealliance.org or 401-369-4017.

Sincerely,

Hakon Heimer
Co-Founder

Cure Alzheimer's FUND

34 Washington Street, Suite 200
Wellesley Hills, MA 02481
ph 781-237-3800
www.curealz.org

February 10, 2015

The Honorable Fred Upton,
Chairman,
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette,
Member,
House Energy and Commerce Committee
Washington, DC 20515

Sent via e-mail: Cures@house.mail.gov

Re: 21st Century Cures Act Discussion Draft

Dear Chairman Upton and Representative DeGette:

Please accept these comments from Cure Alzheimer's Fund about the 21st Century Cures Initiative. Although Cure Alzheimer's Fund applauds the House Energy & Commerce Committee for their attention and commitment to improving biomedical research and drug development, there are a number of provisions in the Discussion Draft that cause concern for Cure Alzheimer's Fund.

Cure Alzheimer's Fund is a national nonprofit that supports research into the genetics of Alzheimer's disease. Cure Alzheimer's Fund believes you cannot know the cure until you know the cause. It was a Cure Alzheimer's fund supported project that mapped the Alzheimer's genome, which was ranked by Time/CNN as one of the Top Ten Medical Breakthroughs of 2008.

Recently, there was attention for the "Alzheimer's in a Dish" initiative which reproduced a human "brain" in a laboratory setting. This Cure Alzheimer's Fund supported research will allow researchers to be able to test numerous already approved compounds to determine if they may have a positive impact on Alzheimer's patients.

The researchers from across the United States who worked on these, and many other, initiatives receive support from private organizations, as well as public support from the National Institutes of Health (NIH). Cure Alzheimer's Fund believes that these public-private partnerships are vital to discovering disease cures. Cure Alzheimer's Fund also believes that all research resulting from its efforts should be public and readily accessible to all.

Because of this, Cure Alzheimer's Fund agrees with the Committee's desire to improve research and data access and transparency. However, the sections of the Discussion Draft focused on NIH, and on the proposed Longitudinal Study, do not seem to meet this goal. Specifically, Cure Alzheimer's Fund would suggest the following sections be removed from the final bill:

- TITLE II: SUBTITLE N- 21st Century Century Chronic Disease Initiative Act

- TITLE II: SUBTITLE O- Helping Young Emerging Scientists
- TITLE IV: SUBTITLE A, Section 4001- NIH Research Strategic Investment Plan
- TITLE IV: SUBTITLE A, Section 4004- Increasing Accountability at the National Institutes of Health
- TITLE IV: SUBTITLE A, Section 4005- GAO Report on Common Fund

Cure Alzheimer's is pleased to see that the language for the Longitudinal Study proposed in Title II Subtitle N has been changed to remove many of the most problematic aspects, but the inclusion of this study still raises concerns. As we have shared with Committee staff, there was a lack of involvement of, or consultation with, academic researchers in the design of this proposed study. The researchers supported by Cure Alzheimer's Fund agree that this proposed study, even with the changed language, will do little, if anything, to advance Alzheimer's research. There are already a number of longitudinal studies underway, and with a stated goal of preventing or effectively treating Alzheimer's disease by 2025, a long-term longitudinal study will provide no value to that effort.

The lack of involvement of academic researchers is the reason that Cure Alzheimer's Fund asks for the removal of the sections listed above focused on NIH. These sections also appear to suffer from a lack of academic researcher insight in their development.

NIH, as well as Cure Alzheimer's Fund must have scientific freedom and integrity as the hallmark of grant selection. Yes, the process can be reviewed to be made more efficient, but Cure Alzheimer's Fund believes these sections do not improve the process, but rather inject non-scientific considerations into the awarding of NIH grants. This is a very dangerous path to pursue. Peer-review has been, and must continue to be, the basis by which grants are awarded by NIH. It is the only way to ensure that the best science is funded.

Although these sections are well-intentioned, the lack of academic researcher involvement in their development raises concerns that these sections, if implemented, instead of improving NIH, could have the opposite effect and in fact weaken not only the grant process at NIH, but also further burden already limited resources at NIH.

Cure Alzheimer's Fund has offered to Committee staff to organize a phone call or meeting with academic researchers so they can share their concerns directly. This is something Cure Alzheimer's Fund would still like to arrange if the Committee has an interest. Cure Alzheimer's Fund does believe it would be quite valuable to hear from academic researchers, or those who will be directly impacted by these proposed sections.

Please feel free to contact Tim Armour, President & CEO of Cure Alzheimer's Fund at 781-237-3800 or tarmour@curealz.org with any questions or concerns.

Thank you for reviewing these concerns. Cure Alzheimer's Fund looks forward to working with the Committee as the legislative process continues to improve on the Discussion Draft and include the insights of academic researchers.

Sincerely,

[redacted]

Tim Armour
President and CEO
Cure Alzheimer's Fund

CuresWithinReach

CUREACCELERATOR™

January 27, 2015

Congressman Fred Upton
2183 Rayburn House Office Building
Washington, D.C. 20515

Congresswoman Diana DeGette
2368 Rayburn House Office Building
Washington, DC 20515

Re: Support for and Addition to the 21st Century Cures Initiative

Dear Representatives Upton and DeGette-

I am proud to be an American every day, but especially proud when I see our elected officials working across the aisle on simple and sensible legislation to solve critical issues that affect family, friends and colleagues here, and around the world. The need to create treatments for the 7000+ unsolved diseases is one of the most critical. Thank you to the two of you for tackling this.

I am personally supportive of your legislative efforts, and so is the non-profit I lead, Cures Within Reach. We will do whatever we can to support the five pillars of your 21st Century Cures Initiative:

1) modernize clinical trials to streamline the approval of drugs and devices;
2) better integrate the patient perspective into the regulatory process;
3) promote better access to and sharing of information such as genomic and other clinical data to foster more collaboration among researchers;
4) invest in the future of science; and
5) better incentivize new drugs and devices for unmet medical needs.

After reviewing as much of the information we could find on your 21st Century Cures Initiative, and the white paper and draft legislation released today, we suggest stronger emphasis for one component mentioned several times in Title I, that would provide greater speed, efficacy and affordability to the patient impact that your legislation will create: REPURPOSING!

Repurposing, as you know, is the quest to quickly and inexpensively create safe, effective and affordable treatments by taking drugs, devices, nutriceuticals, diagnostics and other therapies approved for human use in one disease, and testing them clinically to prove a "new" treatment in a currently unsolved disease.

Cures Within Reach is the leading global organization dedicated to repurposing research. Since 2005, Cures has funded medical repurposing research, working to improve clinical care. The researchers and clinicians we have supported have created over a dozen repurposed therapies that are either being used off-label in clinical care right now, or have received government funding for a larger confirmatory clinical trial in preparation for FDA approval.

With the help of a grant from the Robert Wood Johnson Foundation, we are currently launching CureAccelerator™, the world's first non-profit interactive, online platform dedicated to repurposing research. By connecting researchers, funders, the biomedical industry and patient groups, CureAccelerator will propel the pace of repurposing research, to drive more treatments more quickly to more patients. A representative from NCATS sits on our Advisory Board for this project, and the NIH has made database resources and other expertise available to us to support the success of this platform.

Repurposing could either be a 6th pillar of the 21st Century Cures Initiative, or it could be a featured component of the other five.

Repurposing represents a huge untapped resource pool for the rapid creation of safe and effective treatments and cures. There are over 3000 drugs approved for human use, and another 3000 nutriceuticals that have strong biologic activity and have been used safely by millions of people. Add to that a large number of medical devices and other human approved non-drug therapies, and these resources can be combined with the expertise of thousands of scientists and clinicians armed with published and unpublished data, bioinformatics tools, and clinical and scientific observations, to create a machine that could produce an almost unlimited number of scientifically sound repurposing ideas that are one step away from patient impact.

The missing ingredient to get this repurposing machine running at full speed is a robust market incentive. There are no natural economic industry incentives for most repurposing, since generic drugs and devices, and nutriceuticals, are inexpensive and widely available. No single manufacturer exists, so any physician can use a repurposed therapy off-label, even if someone holds a solid method of use patent. And the government has not created any governmental incentives for the repurposing of generics-until, perhaps, they are introduced in the 21st Century Cures Initiative.

Cures Within Reach is currently working on two ideas to financially incentivize repurposing:
1) to use the healthcare cost savings generated by utilizing effective and inexpensive repurposed treatments to pay back the investors who fund the initial Repurposing Research proof of concept clinical trials. I have attached an executive summary of the potential for using this Social Finance concept to create a market incentive.

2) to create a tiny, tiny tax on each prescription filled at the pharmacy to create a pool of funds for generic Repurposing Research. Almost four billion prescriptions are written in the US each year. A tax

of $0.05 per prescription would raise $200,000,000 per year for repurposing research. That would be enough to create at least 80-160 “new” effective and safe repurposed therapies for unsolved diseases. Based on our most conservative calculations, that investment would yield at least 10 times that much in yearly healthcare savings. And this could be duplicated each year for a long time.

The opportunity is significant, the cost to get started is low, the repurposing machine is primed to get moving, and the need is huge. Let’s figure out what we can do together to move this forward.

Happy to help out in any way necessary. Thank you and the House Energy and Commerce Committee for taking this on!

Sincerely,

[redacted]

Dr. Bruce E. Bloom
President and Chief Science Officer
Fellow, Ashoka Innovators for the Public

Depression and Bipolar Support Alliance

February 10, 2015

The Honorable Fred Upton
Chairman
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Re: Comments regarding the 21st Century Cures Discussion Draft

Dear Chairman Upton:

The Depression and Bipolar Support Alliance (DBSA) applauds the House Energy and Commerce Committee's recent 21st Century Cures Act discussion document. We especially appreciate the inclusion of patient-centered perspectives into the regulatory process. As the nation's preeminent education, support, and advocacy group by and for people living with depression and bipolar disorder, DBSA respectfully submits the following comments that we hope will help the Committee to develop legislation that can effectively engage people who have these conditions in the development of treatments and cures.

About DBSA

DBSA is the leading peer-directed national organization focusing on mood disorders: depression and bipolar disorder. These serious, all-too-often life-threatening—yet also highly treatable—conditions combine to affect more than 21 million American adults, cost an estimated $23 billion in lost work productivity, and account for 90 percent of the nation's suicides every year.

Unlike any other organization of its kind, DBSA is created for, and led by, individuals who themselves have a mood disorder diagnosis, with our bylaws stipulating that over half of both the governing board of directors and paid professional staff must be people who have, or have had, depression or bipolar disorder. This first-person lived experience informs everything that we do.

DBSA's vision is wellness for people with mood disorders, and we believe that an open and collaborative approach to treatment that accounts for the whole person—where she or he is *right now*—is what allows people to achieve what they personally define as wellness. Our collaborators include a Scientific Advisory Board made up of the nation's leading clinical and research experts on mood disorders. We are nationally recognized for Peer Specialist training services, which weave those of us with lived experience of mental health conditions into the fabric of care as adjunctive providers of education and support. DBSA also has a long history of providing cutting-edge, interactive online tools and resources that allow individuals to understand, choose, manage, and evolve their treatment plans. Ultimately, we at DBSA believe that our balanced, person-centered,

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wellness-oriented approach is what has allowed us to educate, empower, support, and inspire individuals to achieve the lives they want to lead for our now-30 years in existence.

Moreover, these three decades of peer-led work have enabled DBSA to coalesce a strong base of active participants. In fact, through the more than 700 free, in-person peer support groups provided by DBSA's network of 300 chapters across the country, along with our printed and virtual educational resources and wellness tools, DBSA reaches over three million people each year with current, readily understandable information about depression and bipolar disorder; connections to treatment and community resources; and—crucially—the hope that wellness is possible.

To fortify our peers' hope, DBSA celebrates the accomplishments of people with mood disorders, including those of the many talented, successful individuals recognized by the public for their contributions to the world. We also promote hope as we seek to advance learning through research. It is at the intersection of hope, personal lived experience, and research that we feel certain DBSA and the Committee can collaborate powerfully.

Innovation and the Incorporation of the Patient Perspective

DBSA applauds the Committee's inclusion of the patient and person-centered perspective into the process of reforming and creating regulations that affect them. For people who have mood disorders, the past 25 years have seen anemic progress in the development of meaningful new treatments. Innovation has been incremental. People electing such treatment are consequently frustrated by, and losing hope of, a pharmacologic solution. Modest improvement in clinical outcomes is simply no longer enough.

Of course the first priority for treatment is ensuring that a person living with depression or bipolar disorder is provided a pathway out of crisis and onto stability. However, all too often, this baseline stability is also the end goal established for successful long-term care. "Stable" or "better" are not always synonymous with "well."

DBSA believes that every person deserves the opportunity not just to *survive* - but to *thrive*, and to do that, we need to ensure true wellness as the end-goal for mental health treatment. Consider this: successful treatment for cancer targets the removal of every cancerous cell—the achievement of complete remission. Why, then, do we consider treatment for depression or bipolar disorder to be successful when symptoms persist, even if the person is considered to be stable? The cost of settling for reduced symptoms is simply too great. And for many, it can be a matter of life and death.

There are many different definitions of collaborative care, but an essential component is shared decision-making between a clinician and patient. Because DBSA believes such shared decision-making is vital to achieving wellness, we support initiatives that foster open dialogues between

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people who live with mood disorders and clinical communities in an effort to improve the quality of mental health care.

When treatment plans are created jointly and in equal partnership between people who live with mood disorders and those who treat them, individuals are more invested in, served by, and able to achieve those plans. By encouraging the collaborative care model, we hope to foster a more person-centered approach that improves the effectiveness of treatments for people living with mood disorders.

We believe that your efforts can push the whole of HHS to work even more collaboratively with groups of patients and providers to identify outcomes that matter to patients. Such efforts could transform those outcomes into rigorous measures, which could then be applied to research and value-based assessments of new delivery models being promoted by CMS. Such work will require a proactive approach within government agencies to solicit the input of patients, as is being done actively at the FDA, accompanied by the effective translation of the patient perspective into the delivery of public health programs. DBSA urges the Committee to require HHS to develop an infrastructure for meaningful patient engagement in all of its agencies, and to demonstrate to Congress how its engagement activities are making a difference in the management of its programs.

Using Patient Experience Data to Enhance Risk-Benefit Assessment Framework

DBSA strongly supports the development and use of patient experience data to enhance structured risk-benefit assessment frameworks at the FDA**.** As the committee works through the complexities and details of these policies, we urge continued engagement of patients and providers, with an explicit goal of facilitating effective shared decision-making.

In particular, we applaud the Committee's focus on using data from patient experiences when considering new drug therapies. Changing measurement tools to include wellness outcomes as defined by people with depression and bipolar disorder would greatly improve those therapies. For example, the FDA could elevate the importance of existing clinical measurement tools that address function, such as the Sheehan Disability Scale, and/or that address wellness, such as the WHO-5 Scale. Both are useful in allowing not only for the mood-related improvements necessary to achieving complete wellness, but also the interpersonal and relational aspects of individuals' experiences of depression or bipolar disorder.

Success should not be defined by controlling this week's, month's, or even year's episode of a mood disorder, but by reducing the severity and eliminating the reoccurrence of symptoms over the entire lifetime. This is not often the defined objective for clinicians or researchers, but it is of vital importance to people experiencing depression and bipolar disorder, as well as their families. DBSA

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envisions exploration of chronic versus episodic experiences of mood disorders and how treatments may need to differ for the chronic recurrence of mood symptoms.

Added Funding for NIH BRAIN Research

We understand that funding for public research generally falls under the jurisdiction of the Appropriations Committee. However, we strongly support and greatly appreciate the Committee's inclusion of additional funding authority for Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative (TITLE IV: SUBTITLE A Section 4008). This program is already providing researchers with innovative tools to identify new ways to treat, prevent and even cure brain disorders. Due to their widespread impact on the Nation, we urge the Committee to direct NIH and researchers to specifically include Depression and Bipolar Disorder participants in studies.

Advancing Research for Neurological Diseases

Research indicates that major depression and bipolar disorder can often result from neurological diseases and we support the discussion draft's creation of a "National Neurological Disease Surveillance System." Like multiple sclerosis and Parkinson's diseases, Major Depressive Disorder (MDD) and Bipolar disorder have demonstrated the capacity to physically change the configuration of the brain. Accordingly, DBSA asks that MDD and Bipolar disorder be included in the expanded infrastructure to track the epidemiology of these serious diseases.

Conclusion

On behalf of our members and the millions of Americans who face mental health challenges every day, we thank you for the considerable time and effort you have put into this important legislative process, and look forward to the eventual passage and enactment of 21st Century Cures legislation and the promise it holds for the Nation.

Sincerely,

[redacted]

Allen Doederlein
President
Depression and Bipolar Support Alliance

Cc: The Honorable Frank Pallone, Ranking Member, Energy & Commerce Committee
The Honorable Diana DeGette

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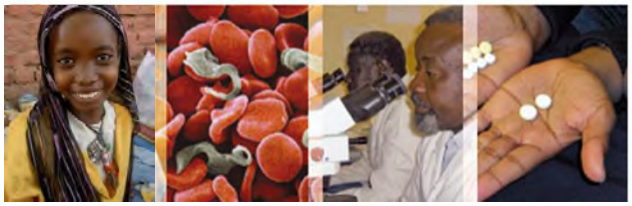
DNDi NORTH AMERICA
Drugs for Neglected Diseases *initiative*



February 20, 2015

The Honorable Fred Upton
Chairman
House Energy and Commerce Committee
2125 Rayburn House Office Building
United States House of Representatives
Washington, DC 20515

The Honorable Frank Pallone
Ranking Member
House Energy and Commerce Subcommittee
on Health
United States House of Representatives
2415 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton and Representative Pallone:

On behalf of the Drugs for Neglected Diseases *initiative* (DND*i*), thank you for the opportunity to comment on the 21st Century Cures draft legislation. As an international not-for-profit, patient-centered research and development (R&D) organization that discovers and develops new, improved, and affordable medicines for neglected patient populations, DND*i* is acutely aware of the need to accelerate the discovery, development, and delivery of new health technologies for a wide range of diseases. Current R&D efforts are woefully insufficient and additional incentives, new financing, as well as novel regulatory pathways are urgently needed to ensure both accelerated innovation and rapid access to medicines and other essential health tools, especially for poor, vulnerable, and marginalized patients who have historically been abandoned by the market.

DND*i* was established in 2003 by Doctors Without Borders/Médecins Sans Frontières (MSF), and six public sector research institutions. Today, DND*i* has more than 30 projects in our pipeline, and has delivered six new treatments that are already in the hands of millions of patients: two fixed-dose anti-malarials; a combination treatment for late stage sleeping sickness; a combination treatment for visceral leishmaniasis in Africa; a set of combination therapies for visceral leishmaniasis in Asia; and a pediatric dosage form of benznidazole for Chagas disease.

DND*i* accomplishes its work through collaborative partnerships with public sector research institutions, particularly in disease-endemic countries, pharmaceutical and biotechnology companies, academia, non-governmental organizations, and governments worldwide. It also works to strengthen research capacity in disease-endemic countries and to advocate for increased public responsibility for neglected disease R&D.

Based on our experience as a needs-driven R&D organization, and given that this legislation could have far-reaching implications beyond even the discovery, development, and regulatory approval of medicines in the United States, we would like to offer comments regarding certain sections of the 21st Century Cures draft legislation.

Modification to the Priority Review Voucher Program for Tropical Diseases
Title IV, Subtitle C, Section 4045 of the draft legislation "rolls in" previous legislation related to the priority review voucher (PRV) program. The PRV program was launched in 2007 to incentivize R&D for certain neglected diseases by rewarding a developer that successfully registers a treatment for specific neglected diseases with a voucher for "priority review" with the Food and Drug Administration (FDA) of a subsequent drug application. To date, only three PRVs for neglected diseases and one for a rare pediatric disease have been awarded since its inception.

We are supportive of the draft language to provide an alternative to the lengthy formal rule-making process for adding or changing the list of diseases that are eligible under the PRV program. However, we are concerned that, based on the experience to date, the PRV mechanism, in its current design and application, is not fulfilling the intended goal of ensuring the development of neglected disease treatments that are accessible to those who need them. There are some key issues that limit the effectiveness of the PRV for neglected diseases as currently designed that we hope can be addressed in the next version of legislation; namely, (a) a PRV can be granted without any new R&D investments; (b) the PRV rewards successful FDA registration, even if that drug is already on the market in other countries; (c) a PRV can be awarded even when public health treatment needs have not been met by the entity receiving the award; and (d) the PRV does not include any mechanism to ensure patients will have affordable and appropriate access to products for which a PRV has been awarded.

The recent case of a PRV awarded to Knight Therapeutics for miltefosine, a visceral leishmaniasis treatment, highlights these concerns (see our recent blog post with MSF in *PLoS Speaking of Medicine* for further details).

Extending Market Exclusivity
Today, companies that receive approval for new drugs in the U.S. enjoy long periods of market exclusivity, during which they are "protected" from generic competition: this period is five years for new chemical entities (NCEs), seven years for rare/orphan disease drugs, and 12 years for new biological medicines. Various provisions in Title I, Subtitles L, M, and N would provide additional market exclusivity, including a proposal for the extension of the exclusivity period to 15 years for drugs for "unmet medical needs."

As an entity that daily faces the challenges of developing drugs to address unmet patient needs we must strongly caution that extended exclusivity only increases barriers to access and delays availability of affordable treatments for neglected populations in desperate need. We strongly oppose provisions in the draft legislation aimed at expanding market exclusivity. This includes provisions in Section 1241 that would extend market exclusivity for two additional years for modifications of existing drugs meeting certain criteria as well as provisions in Section 1063 that would allow for "sale" of "qualified infectious disease product" drug exclusivity to another company.

Antibiotic Drug Development
The draft 21st Century Cures legislation effectively "folds in" two previous pieces of legislation, the Antibiotic Development to Advance Patient Treatment (ADAPT) Act and the Promise for Antibiotics and Therapeutics for Health (PATH) Act, aimed at accelerating the discovery and development of new antibiotics to address the growing global crisis of anti-microbial resistance (AMR). AMR is one of the most important global public health threats today, and the few recently approved antibiotics are simply

not adequate to address the resistance crisis. New approaches are certainly needed to address the dearth of innovation in this field. However, the most important bottlenecks, which are scientific, will not be overcome by the proposals contained in Title I, Subtitle D; in fact, the current FDA approval process may be severely compromised by these proposals, placing patient safety at risk.

Although our comments above are aimed at what we see as the most harmful provisions contained in the draft 21st Century Cures Act, there are other proposals that are interesting and that may have tangible positive benefits when it comes to R&D for neglected patient needs. These include proposals to improve access to clinical trial data, in particular sharing of data generated through publicly-funded research; lifting of the "phase IIb" restriction for the National Center for Advancing Translational Sciences (NCATS) at NIH, which is a step in the right direction that would enable NCATS to invest further downstream in the R&D process; and creation of a "global pediatric clinical trial network" to address the specific and neglected drug development needs of children, a challenge with which DND*i* is all-too familiar, having developed age-adapted formulations for children with malaria and Chagas disease as well as coordinating R&D projects to ensure availability of pediatric formulations for children with HIV/AIDS, sleeping sickness, and a range of other neglected diseases.

DND*i* urges lawmakers to seriously explore policy approaches to accelerate the discovery, development, and regulatory approval of needed drugs and other health technologies that resolve the trade-off between innovation and access, that put in place alternatives to high prices to finance and incentivize R&D, and that do not compromise on patient safety.

We look forward to working with the Committee in the coming months to explore ways in which the U.S. can contribute to achieving the twin goals of accelerating innovation while guaranteeing equitable access to the fruits of scientific research. Please know that DND*i* is more than happy to serve as a resource to you and your staff as this legislation moves forward. Should you have questions or require additional information, please feel free to contact me directly at 646.824.3064 or rcohen@dndi.org, or Jodie Curtis, our Washington representative at 202.230.5147 or jodie.curtis@dbr.com.

Thank you for your consideration of these comments.

Sincerely,

[redacted]

Rachel M. Cohen
Regional Executive Director

cc: The Honorable Diana DeGette
The Honorable Joe Pitts
The Honorable Gene Green
The Honorable Renee Ellmers
Members of the House Energy and Commerce Subcommittee on Health

The Honorable Fred Upton, Chairman
The Honorable Diana DeGette
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515

February 10, 2015

Dear Mr. Upton and Ms. DeGette

The Endocrine Society and the Society for Women's Health Research (SWHR®) were extremely excited to review the 21st Century Cures Discussion Document. Having closely followed the 21st Century Cures initiative and provided input from its inception, our organizations recognize that this document is an extraordinary synthesis of stakeholder expertise and input. We applaud the 21st Century Cures team for their effort and appreciate the opportunity to continue to provide feedback on how to implement transformative change to more efficiently bring cures to the public.

While the 21st Century Cures Discussion Document contains many commendable initiatives, our societies are concerned that the document lacks language to codify a process to include sex differences in basic research at the National Institutes of Health (NIH). This is an imperative provision to meeting the goals of the path to 21st Century Cures. As we and others have noted, biomedical research has historically utilized male research subjects disproportionately, creating a significant gap in knowledge regarding the extent to which disease processes and underlying physiology are influenced by biological sex[1]. The lack of inclusion of females in pre-clinical basic research has resulted in an increasing number of treatments that have had more adverse effects in women and in some cases resulted in medications being pulled from the market.

The NIH has recognized this gap and announced policies to balance the study of males and females in preclinical research[2].With this announcement, the NIH has begun to take steps towards achieving equity in biomedical research, but it has not implemented any of these policies. Therefore, legislation is necessary. We fully support the NIH in this endeavor and we believe that 21st Century Cures could provide the NIH with an incentive to prioritize and accountability to ensure the development and full implementation of these policies. The attached document

[1] Endocrine Society Letter to Bipartisan Group of Women Senators on Sex Differences in Preclinical Research - May 12, 2014. Accessed February 8, 2014.
[2] J.A., Collins, F.S. NIH to balance sex in cell and animal studies. Nature. 509, 282-283 (2014)

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"Codifying a Process to include Sex Differences in Basic Research within NIH" contains proposed language for 21st Century Cures that would give NIH the authority to implement the policies that it is already planning to advance. This language could most appropriately be included in Title IV, Subsection A, of the 21st Century Cures discussion draft.

We believe that a necessary component of any overarching strategy to "build the foundation for 21st century medicine", as 21st Century Cures is capable of doing, should advance the science of sex differences, so we can achieve cures for the entire population. We hope that you will include the attached provision in the 21st Century Cures Initiative. Thank you for your time and consideration. We look forward to working with you to advance the biomedical research enterprise in a truly transformative way.

Sincerely,

[redacted]

Richard J. Santen, MD
President
Endocrine Society

[redacted]

Phyllis Greenberger, MSW
President and CEO
Society for Women's Health Research

Codifying a Process to include Sex Differences in Basic Research within NIH

Background

More than anything, "good science" is at the heart of basic research. It is imperative that data collected be both reproducible and generalizable, because it is this data that leads to important discoveries and breakthroughs. The generalization of data requires that all stages of the biomedical research cycle include a consideration of sex differences in research subjects where appropriate. A significant component of the rigor and completeness in research is the investigation of sex specific effects. Despite decades of awareness of the issue, women are still inadequately represented in many clinical trials. Additionally, sex differences are still not routinely considered as a critical variable in basic biological studies. This critical inconsistency in the biomedical research pipeline can have serious consequences. For example, of the 10 drugs that were withdrawn from January 1, 1997 through 2001, 8 posed greater health risks for women[3]. The consideration of sex is an important biological variable and therefore must be incorporated into preclinical research.

The Office of Research on Women's Health's (ORWH's) Strategic Plan, published in September 2010, included as its first goal to "increase sex differences research in basic science studies." It noted that "an expanded conceptual framework is needed that explores variations due to sex as an integral part of the search for knowledge across the entire research spectrum, beginning at the most basic laboratory level."

In May 2014, NIH Director Collins and ORWH Director, Jeanine Clayton published a comment in *Nature* indicating that it was developing "policies that require applicants to report their plans for the balance of male and female cells and animals in preclinical studies in all future applications, unless sex-specific inclusion is unwarranted, based on rigorously defined exceptions." They indicated that they would be rolling out these policies starting in October 2014. While NIH has initiated this process, we believe that codification of the recommendations below will provide guidance to the process.

Proposed Legislation

1. Authorize NIH to develop policies that require research applicants to report their plans for the inclusion of male and female cells and animals in preclinical studies in all future applications, unless sex-specific inclusion is unwarranted, based on rigorously defined exceptions. No later than one year after enactment of this legislation NIH shall publish the draft policy via a notice of proposed rulemaking to allow for public comment and response. The expansion of such current policies shall include plans for:
    a. Investigators to prominently indicate the sex of their experimental model in their grant application and progress reports.

[3] http://www.gao.gov/new.items/d01286r.pdf Accessed May 20, 2014

b. Investigators studying one sex, should provide justification as to why the study is limited to one sex as a part of the grant reporting process and in published reports. When studying both sexes, investigators should report, and when appropriate, analyze their data by sex as part of grant progress reporting to the Agency and in published results.
c. Investigators to consider sex as a biological variable in relevant research on animals, cells, and human subjects.

2. Direct NIH to monitor compliance of sex and gender inclusion in preclinical research funded by the agency through data-mining techniques that are currently being developed and implemented. Encourage NIH to work with publishers to promote the publication of such research results**.**

3. Authorize the Director of the NIH to establish a Trans-NIH Working Group on Sex Differences in Research, which shall be comprised of representatives of each Institute and Center, the Office of Research on Women's Health, as well as appropriate members of the scientific and academic communities and patient organizations as determined by the NIH Director.

The Working Group shall ensure appropriate implementation of the regulations proposed above; determine the progress of NIH's strategic plan on sex difference in research and to ensure open collaboration between ICs on this matter. The Working Group shall provide a written report to the Director to be included in the NIH biannual report that details the inclusion of females and advances in sex differences in pre-clinical research and include the proportion of women and minorities as subjects in clinical research participant enrollment by trial phase and in all studies of human subjects, the proportion of studies that incorporate sex as a biological variable and of those studies which analyze data by sex as part of grant review, award, and oversight processes and this data should be reported by Institute and Center across the Agency.

4. The National Library of Medicine is urged to implement changes to Clinicaltrials.gov that will require users to input the number of participants that drop out of trials and break those participants out by sex/gender and race.

5. Authorize the Specialized Centers of Research on Sex Differences program, which is a collaboration between ORWH and FDA. The purpose of the program is to "support interdisciplinary collaborations on sex and gender influences in health, and bridges basic- and clinical-research approaches. This program also facilitates training in sex and gender considerations in experimental design and analysis."

FasterCures
A CENTER OF THE MILKEN INSTITUTE

February 13, 2015

The Honorable Fred Upton
Energy and Commerce Committee
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Diana DeGette
Energy and Commerce Committee
U.S. House of Representatives
2368 Rayburn House Office Building
Washington, D.C. 20515

Sent via e-mail: cures@mail.house.gov

RE: Comments on the 21st Century Cures Discussion Document

Dear Chairman Upton and Representative DeGette,

Thank you for the opportunity to provide comments on the discussion document distributed by the Chairman on January 27, 2015 under the 21st Century Cures Initiative. In the days since its release, we have reached out to our network of thought-leaders from patient organizations, industry, academia, and healthcare institutions, including our senior fellows and members of our various advisory councils, to benefit from their insights about the proposals put forward in the draft.

FasterCures shares your goal of bringing efficiency to biomedical R&D by identifying and eliminating the roadblocks that slow progress, and paving a path of meaningful engagement between patients and every sector of the research enterprise. We are pleased that our view of patients as partners is aligned with the patient-focused theme of the first title and provisions throughout the draft document. As a leading voice in bringing together patients and participants across the research ecosystem, *FasterCures* welcomes the opportunity to review the discussion document and outline some overarching issues, as well as provide specific comments. Given our depth and breadth of experience in patient engagement in drug development, we are also developing proposed alternative legislative language for the Committee's consideration on Title I Subtitle A, Patient Focused Drug Development, with a goal of sharing it with the Committee by the end of February.

We have organized our attached comments by title and subtitle of the draft document, focusing on areas where our perspective and content expertise might be most useful to the Committee. Our comments fall into the following general themes:

- *FasterCures* appreciates the focus on patients and would like to ensure the inclusion of patient perspectives through all aspects of medical product development and regulatory decision-making;
- New statutory responsibilities outlined in the draft will need to be accompanied by new resources so that these proposals do not divert scarce resources from existing core responsibilities; and,
- Provisions of the discussion document create new commissions, advisory bodies, reports, studies, and guidance documents. We are concerned that some of these requirements may overlap or be duplicative of current efforts or existing documents. We have available as a resource, should it be helpful, a spreadsheet that compiles all these new requirements.

We would like to use this opportunity to renew our call for stable and robust funding for NIH and FDA, a crucial issue for stakeholders across the research enterprise. We are active members of United for

Medical Research and the Alliance for A Stronger FDA and we will be working closely with them on appropriations.

In addition, we would like to renew our proposal to the Committee submitted November 12, 2014, to form a public-private-partnership focused on advancing the science of patient input. In addition to addressing the needs implicit in Title I, Subtitle A of the discussion draft, this initiative would provide a robust forum to address challenges arising in the initial planning phases of the Precision Medicine Initiative. A workshop convened this week by NIH on "Building a Precision Medicine Research Cohort" surfaced issues very similar to those raised in the process of advancing patient-focused drug development. We believe a unified effort to develop science-based methods to engage, consent, query, and retain the ongoing participation of patients as R&D partners would strengthen the work of our federal agencies, industry, and patient organizations, and would ultimately benefit public health. Our original proposal is appended to our comments on the discussion document. We would be pleased to work with the Committee and to draft language to develop this proposal further.

We applaud your efforts to date on this important initiative and welcome the opportunity to discuss these comments and to provide additional input as the Committee continues its path toward legislative action on a bill that will generate broad support and, when enacted, will speed medical progress.

Sincerely,

Margaret Anderson
Executive Director

FasterCures specific comments:

TITLE I:

We commend the specific mention of addressing unmet medical need and patient-centered benefit-risk evaluation throughout Title I.

- We support the development of a framework to develop methods and means to collect and apply patient perspectives in the assessments of benefits and risks. We endorse collaborative opportunities outlined in **Subtitle A: Patient Focused Drug Development** (pp. 8-15) to shape guidance on this topic. However, the specific language of this subtitle does not fully meet the intended objective of achieving patient focused drug development and could be strengthened in order to provide greater regulatory certainty about the collection, application, and integration of information about patient experiences, expectations, and tradeoffs. In addition to the recommendations provided below, ***FasterCures* is developing a proposal for alternate legislative language that may better achieve what we understand to be the intended objective.** These comments and our more detailed proposal are based on work through our Benefit-Risk Program and a one-day meeting of experts we convened last fall at our Benefit-Risk Boot Camp.

- Sec. 1001 suggests that the structured assessment of benefit-risk informed by "patient experience data" will be utilized by the agency only for regulatory decision-making following a sponsor's submission of a New Drug Application (NDA), a relatively late stage in the drug development process that follows the completion of multiple clinical trials. This application of "patient experience data" is too narrow, and applied too late in the approval process. Rigorously collected patient perspectives from representative populations have the potential to inform the entire drug development spectrum. Consistent with FDA's repeated statements that "… the medical product review process could benefit from a more scientific, systematic, and expansive approach to obtaining input from patients who are experiencing a particular disease condition," the proposal should reflect that patient perspectives can also inform:
    - the earliest steps of target identification and preferences for benefits and tolerances for harms;
    - testing of new agents in humans to evaluate safety;
    - clinical trial design, including the selection of endpoints, comparators, and exclusionary criteria, as well as to evaluate the burdens of clinical trial participation;
    - analysis of study data to shape further development steps; and
    - post-market review including ongoing safety surveillance, risk communications, and consideration of label changes.
- The use of the term "patient experience data" is open to confusion with other, similar terms. For example, patient experience surveys developed by the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) under direction from the Centers for Medicare and Medicaid Services (CMS) collect information about the patient's experience of hospital care. In other settings the term "patient experience data" is used to refer to retrospective capture of patient experience through diaries and self-monitoring methods.
- To ensure that the type of data covered by the process and guidance documents outlined here, both the term and definition used should encompass a broad range of information that could be beneficial to drug development and regulatory decision-making, including the methods outlined in sections (C) and (D) on page 12, lines 19-25, which are considered separate from patient experience data. We can help to clarify this section in our proposal.
- Regardless of the final definition of "patient experience data," we recommend expressly naming industry as one of the parties collecting such data in the definition of "patient experience data" (p. 10, beginning line 18) and as a participant in the workshops described (pp. 13-14). We believe that a multi-stakeholder process that includes FDA, patient organizations, clinicians, academic researchers, and industry would facilitate development, adoption, and refinement of standards and procedures for capturing patient perspectives and integrating them into medical product development.
- The report required five years following enactment (p. 14) should not be limited to addressing the use and potential improvement of specific measures outlined in the provision. We believe it should be expanded to include an assessment of the agency's overall progress toward patient-focused drug development.

- Finally, FDA may require additional expertise from social scientists, health economists, and outcomes researchers familiar with this type of data in order to appropriately incorporate patient experience data (broadly defined) into medical product reviews and throughout all stages of regulatory decision-making. This notation relates to placeholder provisions in the draft document related to FDA staffing and means by which might be authorized to access and attract specialized expertise.

- We commend inclusion of patient perspectives on benefit-risk as a factor in decision-making in **Subtitle E, "Priority Review for Breakthrough Devices,"** (pp. 72-81) and recommend that it also be included in **Section F, "Accelerated Approval for Breakthrough Devices"** (p. 81).
- To facilitate greater understanding about expanded access programs maintained by sponsors of medical products with active development programs, we support the transparency requirements, including publicly named points of contact and information about decision-making timelines, outlined in **Subtitle G, "Expanded Access"** (pp. 82-83).
- We support **"Subtitle K, Cures Acceleration Network"** to provide the director of the National Center for Accelerating Translational Science (NCATS) with more flexibility to fund projects consistent with the purpose of the Cures Acceleration Network (p. 99). We are also in favor of an increased emphasis on awarding grants and contracts by NCATS for **drug repurposing** as described in this subtitle (pp. 100-101).

TITLE II:

- **Subtitle A, "21st Century Cures Consortium"** (pp. 131-139) proposes to create a new entity independent of the federal government to bring together stakeholders to foster collaboration, establish a strategic agenda, identify gaps and opportunities, facilitate interoperability, and to award grants/contracts to accelerate discovery and development of cures, treatments, and prevention. We believe further definition is needed to clarify eligibility for grantees/contractors as well as how private sector funds will be solicited, contributed, and restricted.
    - The independent organizational status and governance structure follow those of the Patient-Centered Outcomes Research Institute (PCORI). As such, we recommend that the learnings from PCORI be leveraged in terms of building a contract/grant-making entity from the ground up and the appropriate level of staff, infrastructure, and ongoing programmatic evaluation. "PCORI at Three Years," published in the *New England Journal of Medicine*, is an introductory source of information. Further, efforts should be made to leverage effective policies created by existing private-public partnerships such as the Foundation for the NIH, Clinical Trials Transformation Initiative (CTTI), Critical Path Institute, and others. *FasterCures'* analysis of 369 consortia, published in *Science Translational Medicine*, provides some excellent insights about ways to leverage the output of research-by-consortia, as does our Consortia-pedia report.
    - A narrowed mission focus would enhance rapid mobilization of active participants, resources, and success. We believe that the concept we proposed to the Committee in November for a public-private partnership to advance the science of patient input might provide a more focused agenda for such an effort. Our original proposal of November 2014 is appended here.
    - We also recommend including an explicit minimum requirement for patient representatives on the governing Board, as a matter of principle.

- While we are supportive of the intended role and purpose of the proposed **Medical Product Innovation Advisory Commission** in **Subtitle B** (pp. 140-148), we are concerned about the amount of infrastructure support required to establish the commission under this model. MPIAC would review federal policies of NIH, FDA, CMS related to discovery-development-delivery of new medical products with the intent of identifying actions to speed the innovation cycle. Its agenda would be developed in consultation with Congress. However, the manner in which its recommendations might affect legislation, be utilized by the Administration, or impact the 21st Century Cures Consortium (proposed in Subtitle A) is unclear.
- **Subtitle F, "Building a 21st Century Clinical Trial Data Sharing Framework"** (pp. 162-168) proposes initiating an application process to award a contract to a "neutral third party" (unaffiliated with any clinical trials) able to provide funding from government or private sources to compile data from federally-sponsored clinical trials in standardized formats. The success – and viability – of this worthy aim will turn on the caliber of the contractor and the Department's capacity to manage the contract in the absence of performance measures related to funding. In service of the objective for the contractor to serve as a neutral third party (p. 166, line 13), applicants should be required to disclose any interests they have with companies that could materially benefit from the applicant's participation in building the network.
- We support new authorities to expand the use of de-identified Medicare data to improve clinical outcomes as outlined later in **Subtitle F, "Building a 21st Century Data Sharing Framework"** (pp. 168-184) including providing access to this data by qualified researchers without regard to their institutional or commercial affiliation. The proposed change in the privacy standards to conform with HIPAA rather than the Common Rule will remove certain restrictive practices.
- **Subtitle G, "Utilizing Real-World Evidence"** is complementary to the Patient-Focused Drug Development provisions in Title 1, Subtitle A and we encourage consultation with industry, academia, patient advocacy organizations, and disease research foundations to foster use of data from patient registries and observational studies (pp. 193-195). The definition of real-world evidence is sufficiently broad to anticipate the evolution of both the sources and types of data that have utility.
- We support the expansion of the NIH Director's authority under **Subtitle L, "NIH-Federal Data Sharing"** (pp. 206-207) to require grant recipients to share data and believe it could be more explicit to build on the 2003 rule setting an expectation for NIH grantees to share data.
- The ability to **"Access, Share and Use Health Data for Research Purposes"** under **Subtitle M** (pp. 207-214) enhances patients' opportunities to grant use of their data to HIPAA-covered entities for certain specified types of research and we support the intent underlying this provision.
- Large cohort studies are at the center of several provisions in the discussion document, including **Subtitle N, "21st Century Chronic Disease Initiative Act"** (pp. 215-216), **Title IV, Subtitle B, "Advancing Research for Neurological Diseases"** (pp. 255-259), as well as with the President's promising Precision Medicine Initiative proposed in the FY 2016 budget. We look forward to further details about the alignment of the Committee's vision with the Administration's vision for precision medicine, in text that would populate **Title II, Subtitle Q,** "Precision Medicine." This appears to be an opportunity to bring all these cohort-based initiatives together.
- The aim of **Subtitle P, "Fostering High-Risk/High-Reward Science"** (p. 222) may be possible to advance with increased support utilizing existing NIH support mechanisms as was reported in 2014

with 85 awards totaling $141 million made through the NIH Common Fund using New Innovator, Transformative Research, and Early Independence Award programs.

TITLE III:

- We support provisions in **Subtitle A, "Clinical Research Modernization"** (pp. 229-231) to encourage centralized institutional review boards and reduce duplicative effort for multi-site studies. We believe this will reduce administrative burdens and accelerate innovation. We encourage the Committee to draw upon the expertise of entities including CTTI to accelerate ongoing multi-stakeholder efforts and avoid potentially confusing terminology or rules.
- **In Subtitle B, "Broader Application of Bayesian Statistics and Adaptive Trial Designs,"** (pp. 232-235) we support prioritizing the issue of the final guidance from FDA in this area to provide greater regulatory certainty.

TITLE IV:

We support the strategic allocation of resources and performance evaluation and encourage the Committee to work with the Secretary and NIH and FDA leadership to enhance planning and accountability functions, as well as reduce administrative burdens.

- We commend Section 4009 (p. 254) in **Subtitle A, "National Institutes of Health"** to allow NCATS to support phase IIb trials to advance promising therapies further in development.
- We look forward to evaluating the forthcoming language for **Subtitle E, "FDA Hiring, Travel and Training**," as we believe this will be crucially important to the success of many provisions outlined in the discussion document.
- We commend the creation of opportunity for public comment in **Subtitle H, "Local and National Coverage Decision Reforms"** (p. 286). The author's note to seek ways in which national and local coverage decisions can work better for the Administration and patients seeking coverage under Medicare gets to the heart of issues here.
- Similarly, we welcome the measure in **Subtitle P, "Medicare Pharmaceutical and Technology Ombudsman"** to make CMS more accessible by the public, including industry (p. 322).

TITLE V:

- **Subtitle D, "Medical Device Reforms"** (p. 356) again reinforces that registry data be considered as valid scientific evidence and defines a process to establish standards for it. To the extent possible under existing authorities, we recommend harmonizing processes to establish standards for these types of data and evidence for drugs and devices.

FasterCures
A CENTER OF THE MILKEN INSTITUTE

November 12, 2014

The Honorable Fred Upton
Chairman
Energy and Commerce Committee
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Diana DeGette
Member
Energy and Commerce Committee
U.S. House of Representatives
2368 Rayburn House Office Building
Washington, D.C. 20515

RE: Legislative Proposal for the 21st Century Cures Initiative
Sent via e-mail: cures@house.mail.gov

Dear Chairman Upton and Representative DeGette,

As is evident by our name alone, *FasterCures*' mission is tightly aligned with the stated goal of the Committee's 21st Century Cures Initiative, to accelerate the pace of cures. The listening phase of the Initiative has already done just that by inspiring an intense, intelligent, solutions-oriented dialogue about ways stakeholders across the biomedical system can contribute to faster cures. Of course, sustained and full funding of both NIH and FDA are of paramount importance to the success of the biomedical research system and we urge you to work with two groups we are members of on funding issues - United for Medical Research and the Alliance for a Stronger FDA.

We are honored to have been included in formal sessions with the Committee and in dozens of other stakeholder meetings where ideas have percolated and proposals have emerged. Your visionary leadership and the Committee's roundtable discussions and hearings have produced a great deal of consensus from the community about priority areas of promise and action. You have raised awareness and deepened understanding by bringing a wide range of issues and opportunities into sharper focus for lawmakers and constituents alike.

With the Committee transitioning from listening to legislative mode, we offer a proposal focused on the creation of a public-private partnership, an entity we have referred to as the Partnership to Advance the Science of Patient Input. This proposal reflects insights drawn from *FasterCures'* programs dedicated to venture philanthropy organizations, medical research consortia, patient-centered benefit- risk assessment, and value and coverage. It is informed by interactions with patient-based organizations, industry, academia, government agencies, legislative bodies, investors, healthcare professionals, payers, and the public. It builds on key principles articulated in our written statement of June 25, 2014.

In our analysis of the vast landscape of possibilities, the concept outlined here has enormous potential to advance our shared goal of faster cures by developing science-based methods to elicit, quantify, and utilize patient perspectives to inform and influence decisions throughout the full arc of the discovery, development, and delivery cycle. It addresses many of the needs outlined in the Committee's "Call to Action" that launched the 21st Century Cures Initiative. It echoes many other stakeholders' recommendations and priorities and leverages investments made by the federal government and the private and public sectors.

We would be pleased to discuss this proposal and to provide further supporting detail. For the benefit of every American, we urge the Committee to include this concept in its forthcoming legislation to improve the efficiency and effectiveness of the biomedical system and we look forward to working on this in partnership.

Sincerely,

[redacted]

Margaret Anderson
Executive Director

PROPOSAL TO THE U.S. HOUSE ENERGY AND COMMERCE COMMITTEE
Partnership to Advance the Science of Patient Input

Executive Summary: Patient-centricity is heralded as a major innovating force in research and healthcare. However, at present the knowledge about and methods for capturing, analyzing, and utilizing patient input are decentralized and are undergoing rapid evolutionary change without an understanding of their success or impact. A public-private partnership provides the ideal forum to: assess the current state of understanding of the science of patient input; identify gaps and needs; spearhead development of tools, standards, and methods; and guide application to settings across the full arc of the discovery, development, and delivery cycle to fulfill the promise of a patient-focused biomedical system. For purposes of this proposal, we refer to such a partnership as the Partnership to Advance the Science of Patient Input. It is important to note that robust funding for both the NIH and FDA are critical to the success of this type of work. Stable and full funding for these agencies is of paramount importance.

A Shifting Paradigm

There are more than 10,000 known prevalent and rare human diseases and fewer than 10 percent of these have an approved primary therapy. This enormous gap represents serious unmet medical need with millions of patients' lives hanging in the balance. In many of the roundtable discussions and hearings convened under the 21st Century Cures Initiative, individuals representing diverse stakeholder groups spoke persuasively about the promise of a more patient-focused system of biomedical research and care to narrow this gap. Yet until fairly recently, patients and patient groups were considered special interests rather than partners. This is changing, with more patients becoming pro-active participants in the system and more patient-based organizations becoming research engines themselves. Patient-based non-profits are making strategic research investments informed by a detailed understanding of the therapeutic development pipeline. They are building registries, biorepositories, and clinical trials networks. They convene experts to develop care guidelines and accreditation standards and they provide data to payers to improve access to care through informed coverage and reimbursement policies. They are the catalysts for a 21st century of cures.

Research institutions are gaining respect for the content expertise housed in patient communities and they are increasingly interested in engaging patients in the prioritization of basic and translational research to ensure that their needs are understood, their viewpoints are reflected, and their networks are engaged. Two examples of federal funders leading this trend are the Department of Defense Congressionally Directed Medical Research Program's inclusion of consumers in the scientific review of research applications and the NIH's National Center for Advancing Translational Science's formation of a Patient Engagement Subcommittee of its Advisory Council.

The long, costly, and complex process of developing and approving new medical products has traditionally occurred without much direct interaction with patients, aside from the vital role they play as subjects in clinical studies. Some innovative pharmaceutical and biotechnology companies have recognized that bringing patient perspectives closer to all aspects of the research and development enterprise has the potential to focus resources on therapies that patients truly value, potentially saving time and expense. We have seem those efforts grow in recent years.

Congress also recognized the opportunity to benefit from patients' perspectives in regulatory decision-making with passage of the 2012 Food and Drug Administration Safety and Innovation Act (FDASIA) and related user fee agreements that created new programs to expand patient input and consider patient perspectives in the structured assessment of benefits and risks. Increased attention from regulators in patient views will almost certainly spur even more interest from industry sponsors.

In the past, regulatory approval of new medical products defined success. But a new benchmark is achieving a "reimbursable label." This requires sponsors to satisfy payers' expectations for evidence that a medical product improves the way a patient feels or functions when making coverage determinations, a different threshold for some products than regulators require. Demonstrating clinically meaningful benefit can be linked to patient-reported outcomes, but evidentiary standards, even for public payers including the Centers for Medicare and Medicaid Services, are not easy to gauge.

Finally, the Patient-Centered Outcomes Research Institute (PCORI) was created as a provision of the 2010 Patient Protection and Affordable Care Act to improve the quality and relevance of evidence available to help patients, caregivers, clinicians, employers, insurers, and policy makers make informed health decisions. PCORI has involved patients and other consumers in all facets of its planning, implementation, and evaluation and it has made patient engagement a requirement for all research it supports.

These trends have created a new currency for patient data and have intensified the need to sharpen the science of how patient input is collected and made actionable. Stakeholders across the research and care enterprise are working – mostly independently – to define and scale patient engagement, develop instruments to measure patient-reported outcomes, quantify preferences, and incorporate patient perspectives and insights into decision-making processes and work flows. However, there is little documented evidence of successful practices to emulate or failed experiments to avoid that could inform programs, guide resource allocations, or shape policy. Concerns about privacy, conflicts of interest, and other ethical, legal, and regulatory barriers – actual or perceived – add further uncertainty.

The Promise of Partnership

Public-private partnerships (PPP) are neutral forums where entities that represent the interests of society, such as government agencies and non-profit organizations, collaborate with the commercial sector to advance a mutual interest or address a shared challenge. PPPs can be small and temporary or formal and institutional. Successful PPPs are built on a commitment to outputs that benefit the whole, rather than a single group. The structure provides a means to integrate resources and to identify, manage, and isolate conflicts of interest to preserve integrity. The opportunity they provide to pool resources, leverage assets, and access specialized expertise and information in a safe harbor makes PPPs a particularly appealing structure to tackle complex challenges that affect multiple stakeholders. *FasterCures* has spearheaded efforts to characterize these consortia and the metrics for their success through our Consortia programmatic efforts.

The urgent need to bring greater organization and rigor to patient engagement and patient input is one such challenge. A PPP would provide the ideal forum to: assess the current state of

understanding of the science of patient input; identify gaps and needs; spearhead development of tools, standards, and methodologies; and guide application to settings across the full arc of the discovery, development, and delivery cycle to fulfill the promise of a patient-focused biomedical system. For purposes of this proposal, we refer to such a partnership as the Partnership to Advance the Science of Patient Input.

This cross-sector Partnership would provide a neutral collaborative environment to align interests, integrate multiple disciplines and types of expertise, and harness knowledge and data from diverse sources that currently reside in various government departments and agencies, academic and professional organizations, the private sector, and not-for-profit entities. High-level leadership and active participation from the government sector (including the National Institutes of Health, Food and Drug Administration, and Centers for Medicare and Medicaid Services), the private sector (including pharmaceutical companies, biotechnology companies, device companies, diagnostic companies, and private payers), and the public sector (including patients, health care consumers, voluntary health organizations, and academic researchers) will be vital to its success. Partners would contribute human, intellectual, and financial resources and would participate in governing the PPP. A third party manager provides overall program management support, facilitates timely communication between participants, partners, and external stakeholders, and helps to resolve conflicts and questions. The manager also stewards the products of the PPP, monitoring adoption and bringing new opportunities to the attention of the governing body.

The Accelerated Medicines Partnership of the NIH, FDA, 10 biopharmaceutical companies and numerous non-profit organizations, managed by the Foundation for the NIH serves as an appropriate governance model. *FasterCures* can provide additional guidance on a governance structure at the Committee's request; such guidance would be based on its programmatic work in the Consortia-pedia report that documents current practices among more than 400 biomedical research consortia. Defining a formal governance structure will be essential to establish expectations and trust needed to keep participants engaged, as well as ensure a high level of accountability.

Building on Prior Investments

The science of patient input has grown organically in response to a broad variety of needs and specialized interests. Several substantive federal investments in programs designed to capture patient input provide a strong basis for a focused Partnership effort. To highlight a few:

Patient-Reported Outcomes Measurement Information System (PROMIS): Funded by the National Institutes of Health, PROMIS aims to provide clinicians and researchers access to efficient, precise, valid, and responsive adult– and child–reported measures of health and well–being. PROMIS tools measure what patients are able to do and how they feel by asking questions. PROMIS' measures can be used as primary or secondary endpoints in clinical studies of the effectiveness of treatment.

Study Endpoints and Labeling Development (SEALD): Supported by the FDA in the Center for Drug Evaluation and Research, SEALD advances innovation and excellence in clinical trial measurement of treatment benefit. This includes the development and implementation of standards for clinical outcome assessments used as effectiveness endpoints and review policies to provide medical product labeling that is accurate, consistent, and useful.

Patient Preference Initiative: FDA's Center for Devices and Radiologic Health (CDRH) established this initiative to provide the information, guidance and framework necessary to incorporate patient preferences on the benefit-risk tradeoffs of medical

devices into the full spectrum of CDRH regulatory processes and to inform medical device innovation by the larger medical device community.

Registries for Evaluating Patient Outcomes: A User's Guide: This reference published by the Agency for Healthcare Research and Quality (AHRQ), now in its third edition, provides information on the design, operation, and analysis of patient registries. In 2010, the User's Guide was updated with a focus on collecting information to assess patient outcomes.

Some of the other existing resources funded by government, public and private entities are listed in Table 1 at the end of this proposal. It is not intended to be a complete listing, but merely an illustration of the types of existing U.S.-based efforts that support further expansion of this field and its potential to transform the biomedical ecosystem through stronger coordination of efforts and investments. A comprehensive landscape assessment performed as an early step in the Partnership would serve to inventory past investments and existing tools in order to identify and prioritize gaps and needs.

Tools and Processes That Span the Full Arc of Discovery, Development, and Delivery

Building on existing resources, the Partnership would form teams to develop and validate tools such as standards, methods, and instruments to elicit, collect, store, and utilize patient input. Well-defined pilot projects and demonstration models in targeted populations or focused clinical areas are likely to precede more generalizable approaches. Specific projects might be organized according to objectives such as expanding patient participation (as might be useful for a patient registry, clinical trial, prevention program, or surveillance network), measuring meaningful benefit (to determine efficacy, guide product labeling, establish value, or improve adherence), or assessing unmet needs (for making research resource allocations, identifying therapy targets, understanding risk tolerance, or assessing product satisfaction). Of paramount importance will be approaching the development process with the intention of deriving cross-cutting benefits that meet needs across the full arc of the biomedical ecosystem, rather than the interests of any single stakeholder group or participating institution.

Envisioned as an extension of the 21st Century Cures Initiative through authorizing legislation that the U.S. House Energy and Commerce introduces, the Partnership is proposed to have near-term and lasting applications for federally supported activities that improve public health. Specific functions that could be enhanced include the allocation of federal research funds, regulation of medical products, and coverage for healthcare products and services that are more strongly aligned with patient needs, priorities, and expectations. Outputs of the Partnership have potential to inform executive branch programs, policies and rulemaking, yet do not supplant authorities previously granted to federal departments or agencies. The Partnership may also serve as a valuable resource for informing future legislative priorities.

TABLE 1: Existing Resources for Building the Science of Patient Input

Government	Academic & Non-Profit Organizations	Private Sector
Agency for Healthcare Research and Quality: Consumer Assessment of Healthcare Providers and Systems, National Quality Measures Clearinghouse, Registry of Patient Registries and User's Guide to Registries for Evaluating Patient Outcome Measures	Brookings Institution: Enhancing the Use and Development of Patient-Reported Outcome Measures in Drug Development Centre for Innovation in Regulatory Science (CIRS): Unified Methodologies for Benefit-Risk Assessment (UMBRA)	Mayo Clinic: Shared Decision-Making National Resource Center Optum: SF Health Surveys PatientCrossroads: Connect Patients Like Me: Open Research Exchange

CMS initiative Partnership for Patients - http://partnershipforpatients.cms.gov/ Department of Defense Congressionally Directed Medical Research Program: Consumer Involvement program Food & Drug Administration (FDA)-Center for Devices and Radiologic Health: Patient Preference Initiative FDA-Center for Drug Evaluation and Research: Patient Focused Drug Development Initiative and Study Endpoints and Labeling Development FDA-Office of the Commissioner: Patient Representative Program and Patient Network National Cancer Institute: Outcomes Research Branch National Institutes of Health: Patient Reported Outcome Measurement Information System (PROMIS)	Clinical Trials Transformation Initiative: Best Practices for Engagement with Patient Groups in Clinical Trials Critical Path Institute: Patient-Reported Outcomes Consortium and Electronic PRO Consortium Genetic Alliance: Platform Engaging Everyone Responsibly Center for Medical Technology and Policy: Green Park Collaborative International Society for Pharmacoeconomics and Outcomes Research (ISPOR): Outcomes Guidelines Research Index Medical Device Innovation Consortium: Patient-Centered Benefit-Risk Assessments National Health Council: Information Collection Tool for Patient Organizations and Implementation Manual National Organization of Rare Disorders: Registry Platform National Quality Forum: PROs in Performance Measurement Parent Project Muscular Dystrophy: Draft FDA Guidance project Patient-Centered Outcomes Research Institute: National Patient-Centered Clinical Research Network, engagement methodology and patient-centered research methodology	Sanofi: Partners in Patient Health 23andMe: Participatory research

Federation of STATE MEDICAL BOARDS

February 23, 2015

Committee on Energy and Commerce
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton, Ranking Member Pallone, and Members of the House Energy & Commerce Committee:

On behalf of the Federation of State Medical Boards (FSMB), the national non-profit representing the 70 state medical and osteopathic boards of the United States and its territories, I am pleased to submit comments in response to the Energy and Commerce Committee's draft legislation, *21st Century Cures Act*.

Recommendation 1: Sense of Congress Regarding State Medical Board Compact (Subtitle I – Telemedicine, pg. 299)

The FSMB and its Member Medical Boards offer our sincere appreciation to the Energy and Commerce Committee for voicing support for the development and implementation of the Interstate Medical Licensure Compact, a new expedited pathway for qualified physicians seeking licensure in multiple jurisdictions.

In September 2014, following an 18 month drafting process, final model legislative language of an Interstate Medical Licensure Compact was released to states and their respective medical boards for their formal consideration. As of February 23rd, at least 27 state medical and osteopathic boards have formally voiced support for the Compact, as well as the American Medical Association, American Academy of Dermatology, Council of Medical Specialty Societies, Society of Hospital Medicine, and many other health management associations and hospital systems across the nation. We expect the list of supporters and legislative activity to continue to grow as state legislatures begin to formally consider the Compact during the 2015 legislative session. The Compact legislation has already been introduced in 14 states, including Idaho, Illinois, Iowa, Maryland, Minnesota, Montana, Nebraska, Oklahoma, South Dakota, Texas, Utah, Vermont, West Virginia, and Wyoming.

For the purposes of clarity as to the Compact's functionality, the FSMB respectfully recommends that the (c) SENSE OF CONGRESS REGARDING STATE MEDICAL BOARD COMPACTS be rephrased to read:

(c) SENSE OF CONGRESS REGARDING INTERSTATE MEDICAL LICENSURE COMPACT
It is the Sense of Congress that States' enactment of the Interstate Medical Licensure Compact will expand access to care, facilitate multistate practice and enable the use of telehealth services across state lines, by streamlining licensing processes and ensuring the necessary state medical regulatory authority to protect the public.

Recommendation 2: Standard of Care / Definition of Telehealth (pg. 294)

In selecting and defining telehealth services eligible for payment, the FSMB recommends that the Energy and Commerce Committee review and consider the *Model Policy on the Appropriate Use of Telemedicine Technologies in the Practice of Medicine*, adopted unanimously in 2014 by the FSMB House of Delegates. The *Model Policy* defines telemedicine as "the practice of medicine using electronic communications, information technology or other means between a licensee in one location, and a patient in another location with or without an intervening healthcare provider."

Among its key provisions, the model policy states that the same standards of care that have historically protected patients during in-person medical encounters must apply to medical care delivered electronically. Care providers using telemedicine must establish a credible "patient-physician relationship," ensuring that patients are properly evaluated and treated and that providers adhere to well-established principles guiding privacy and security of personal health information, informed consent, safe prescribing and other key areas of medical practice. The guidelines are designed to provide flexibility in the use of technology by physicians – ranging from telephone and email interactions to videoconferencing – as long as they adhere to widely recognized standards of patient care.

The FSMB recommends that legislative language be included in the bill to reflect that providers of payable telehealth services must adhere to the same rules, regulations and laws, as they relate to the standard of care and licensure, of the state where the patient is located, as the provider would in a traditional face-to-face medical encounter.

The FSMB was proud to endorse *H.R. 3750, The Telehealth Modernization Act of 2013*, introduced by Reps. Matsui and Johnson, which establishes a much-needed federal definition of telehealth, and hopes the Energy and Commerce Committee will consider its inclusion in the legislation.

Recommendation 3: Geographic Limitations

The FSMB recommends that language associated with "any geographic limitation" (Pg. 292 and Pg. 297) be clarified as in relation and solely for the purposes of payment, and not in terms of licensure requirements. The FSMB has regularly affirmed that the practice of medicine occurs where the patient is located, rather than where the provider is located. This patient-centered model is both time-tested and practice-proven, and is the nationwide standard that ensures that state medical boards have the legal capacity and practical capability to regulate physicians treating patients within the borders of their state, and to attest that those physicians meet the qualifications necessary to safely practice medicine.

Conclusion

The FSMB commends the Energy and Commerce Committee for its efforts to expand access to telehealth services to patients in a safe and accountable manner. The FSMB would be pleased to meet with you to discuss our recommendations. We thank you for your bi-partisan leadership on this important issue, and look forward to working with you in the 114th Congress.

Sincerely,

[redacted]

Humayun J. Chaudhry, DO, MACP
President and Chief Executive Officer
Federation of State Medical Boards

February 11, 2015

The Honorable Fred Upton
Chairman
House Energy and Commerce Committee
US House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Diana DeGette
US House of Representatives
2368 Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Upton and Representative DeGette:

Genentech, a member of the Roche Group, is a leading biotechnology company that discovers, develops, manufactures, and commercializes medicines to treat patients with serious or life-threatening medical conditions. Americans of all ages, ethnicities, and income levels are prescribed and administered our products. The Roche Group has been actively engaging in life saving treatments and we appreciate the opportunity to comment on the legislative draft of the 21st Century Cures Initiative.

It is evident that a great deal of time and effort has gone into this proposal and for that we are most appreciative. Genentech firmly believes that a strong partnership between industry and government is essential to providing the best and most innovative products for patients. Attached, please find our response to the legislative draft.

Again, thank you for the opportunity to comment. We look forward to engaging with the Committee as it explores different ideas through the 21st Century Cures Act. Should you need any additional information, or if Genentech can assist you in any way, please feel free to contact Evan Morris or Anna Griffin at 202-296-7272.

Sincerely,

Evan Morris
Vice President, Government Affairs
Genentech, a member of the Roche Group

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Sec. 1001. Development and use of patient experience data To enhance structured risk-Benefit assessment framework.	• We agree with the intention to include patient experience data to enhance the structured risk-benefit assessment framework • Broadening the scope of the USPI or creating an altogether new and separate mechanism to provide patients with information that would enable them to make more informed decisions regarding their treatment should be considered. At present, the data included in the USPI are, by statute, directed towards prescribing physicians, however, there is broad consensus regarding the importance of the voice of the patient in treatment decision-making. • Similarly, when looking at the patient label, there is only information on how to use the drug; no data are included that would inform patients regarding	• There needs to be consideration to the process through which sponsors may approach FDA for discussion/decision about the use of PRO data as label-enabling endpoints to ensure that there is sufficient expert input into the discussion and also that a timely decision is reached about the use of PRO data. • It is possible that a process similar to that discussed with respect to biomarkers could also be utilized for PROs. • Report to Congress after 5 years may not be necessary – we would prefer to have the focus be on making progress with respect to developing guidance documents – it may be more beneficial to have up-to-date information on the FDA website about the progress that has	• We are able to assist with discussions on process and procedures that would allow for timely decision-making with respect to PROs similar to the Biomarker Procedures/ Processes discussed in the next section of this chart. • Additionally, we would like to provide technical assistance on the development of novel label-enabling tools to effectively capture the patients' perspective, as we have developed innovative approaches that would allow PRO data to be used for regulatory and clinical decision-making.

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
	what to expect in terms of efficacy (*e.g.*, impact on survival, symptoms or function) or tolerability/treatment burden. Currently, only peer-reviewed publications may be used, and these are often inaccessible to patients; promotional/DTC activities are governed by the content of the USPI, and educational activities are only directed towards health care professionals. • We agree with the need for additional guidance documents on patient reported outcomes. The topics in the bill are helpful – methodological considerations are important. We believe there should be focus on the development of novel label-enabling tools to capture the patients' perspective and on innovative approaches to mitigate bias. Also important are	been made with respect to PROs and incorporating the patient voice into drug development.	

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
<u>TITLE I</u> – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
	strategies for determining disease and treatment burden, function, and use of registries – all noted in the Bill. • We agree with the provisions regarding workshops, guidance documents, and posting of information on the website.		
Subtitle B – Surrogate Endpoint Qualification and Utilization			
Sec. 1021. Evidentiary Standards for the review of requests for the qualification of surrogate endpoints; Biomarkers Partnership.	• We agree that prospective evidentiary standards are essential for the efficient development and regulatory qualification of biomarkers and alternate endpoints, by (1) providing sponsors with clarity and predictability, and (2) ensuring consistency in the Agency's approach to regulatory qualification. • We appreciate that the Agency's evidentiary standards are to be developed in consultation with	• We are concerned that the evidentiary standards required in Sec. 1021 focus only on surrogate endpoints. Developing evidentiary standards for surrogate endpoints *de novo* will be challenging and could result in an unattainable standard. Instead, we believe that evidentiary standards should be developed for the continuum of biomarker use cases, building logically from simpler contexts. We believe this "continuum	• We would like to work with the Committee to develop language that would facilitate the development of evidentiary standards for the continuum of biomarker contexts of use. • We would like to work with the Committee to develop language that would clearly differentiate the processes for qualifying biomarkers from those associated with utilizing biomarkers within the context of individual drug, device, or

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
	external scientific and medical experts, including experts from industry, and are to be issued in draft form allowing for robust public comment. • We appreciate the Committee's recognition that alternate endpoints are most often discussed within the context of individual drug, device, or biological product development programs, and as such, we appreciate the Rule of Construction designed to protect the confidentiality of these discussions with the Agency.	approach" will allow for the logical progression of evidentiary data tied to context of use and will result in a more rational, attainable standard for surrogate endpoints. • While we agree that external scientific and medical expertise is essential for the development of evidentiary standards, as well as for the evaluation of qualification requests, we are concerned that tasking an external public-private partnership with making regulatory determinations for biomarkers and alternate endpoints may (1) undermine FDA's authority, and (2) prevent "buy-in" at the FDA reviewer level.	biological product development programs.
Sec. 1022. Enhancing the process for qualification of surrogate endpoints.	• We support the timelines proposed by the Committee, which we believe will promote a more predictable, efficient	• We are concerned that the focus of Sec. 1022 is solely on surrogate endpoints.	• We would like to work with the Committee to develop language for inclusion in Sec. 1022 "(f) Public Availability of

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
	Qualification Program. • We support the Committee's proposal to allow consultation with external scientific and medical experts and appreciate the safeguards put in place to ensure protection of confidential information. • We appreciate the Committee's commitment to transparency and engagement, as evidenced by the proposed Public Forum. • We support the Committee's proposal to make information publicly available related to applications received, reviewed, and decided upon. Further, we believe this proposal could be adapted to fulfill the reporting requirements proposed under Sec. 1024, which would free valuable FDA resources for mission critical work.	• We believe that all biomarker qualification requests should be considered under Sec. 1022. • We believe it will be essential for the proposed Public Forum to enable informed, timely regulatory decision-making by FDA, and believe there should be rigorous process/procedural controls developed.	Information-" that would ensure metrics necessary to evaluate the performance of the updated FDA Biomarker Qualification Program are collected in a least burdensome manner.

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Sec. 1023. Transitional provisions for previous submissions for qualification of biomarkers as surrogate endpoints.	• We appreciate the Committee's attention to the many biomarker qualification requests currently in the Consultation & Advice stage of the Biomarker Qualification Program. • We support the Committee's attempt to expedite the review and qualification of these biomarkers.	• We are concerned that the focus of Sec. 1023 is solely on surrogate endpoints. • We believe that all biomarker qualification requests should be considered under Sec. 1023.	
Sec. 1024. Biannual reports to Congress.	• We appreciate the Committee's attention to evaluating any proposed changes to FDA's Biomarker Qualification Program. • We agree that metrics that define the performance of the program, as well as its utilization by stakeholders, should be tracked.	• We are concerned that extra reporting requirements will divert valuable FDA resources away from the primary goals of (1) developing and refining evidentiary standards and (2) qualifying biomarkers. • We support the provisions in Sec. 1022 entitled "(f) Public Availability of Information-" and believe these data can be adapted to passively monitor program performance in lieu of additional reporting	• We would like to work with the Committee to develop language for inclusion in Sec. 1022 "(f) Public Availability of Information-" that would ensure metrics necessary to evaluate the performance of the updated FDA Biomarker Qualification Program are collected in a least burdensome manner.

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
<u>TITLE I</u> – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
		requirements.	
Subtitle C – Approval of Breakthrough Therapies			
Sec. 1041. Approval of breakthrough therapies.		• We need more information about what problems this section is addressing.	
Subtitle D – Antibiotic Drug Development			
Sec. 1061. Approval of certain drugs for use in a limited population of patients.	• We support the provisions as outlined in Sec. 1061 and appreciate that the pathway will be applied at the request of the sponsor. • We appreciate that the Committee has taken care to explicitly state that sponsors will not be prohibited from concurrently utilizing existing expedited drug development/review programs. • We greatly appreciate that the provisions in Sec. 1061 apply equally to biologics.		• We are available to support the Committee as they refine this proposal.
Sec. 1062. Susceptibility test			

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TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
interpretive criteria for microbial organisms.			
Sec. 1063. Election to convey a portion of extended exclusivity period applicable to qualified infectious disease products.	• We support the provisions outlined in Sec. 1063. • We greatly appreciate that the Effect of Conveyance is specifically outlined for biological products under proposed section 505E(3)(A)(iv).	• We are concerned that section 505E of the Federal Food Drug and Cosmetics Act (21 U.S.C. 355f *Extension of exclusivity period for new qualified infectious disease products*) does not currently apply to biologics.	
Sec. 1064. Encouraging the development and use of new antimicrobial drugs.	• We support the provisions outlined in subsection (a) of Sec. 1064.	• We encourage the Committee to consider whether the study and report required under subsection (b) of Sec. 1064 is duplicative of the efforts of the Task Force for Combating Antibiotic-Resistant Bacteria outlined in Section 8(a) of the Executive Order on Combating Antibiotic-Resistant Bacteria issued by President Obama on September 18, 2014. We encourage the Committee to examine the remit and progress of the Task Force to ensure the most efficient use of federal resources.	

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<u>TITLE I</u> – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
		• We are concerned that section 505E of the Federal Food Drug and Cosmetics Act (21 U.S.C. 355f *Extension of exclusivity period for new qualified infectious disease products*) does not currently apply to biologics.	
Subtitle E – Priority Review for Breakthrough Devices			
Sec. 1081. Priority review for breakthrough devices.			
Sec. 1082. CMS coverage of breakthrough devices [to be supplied].	• We agree that there is a need for additional innovative regulatory pathways for devices.		• We are available to provide technical assistance (Roche Diagnostics).
Subtitle F – Accelerated Approval for Breakthrough Devices			
Sec. 1101. Accelerated approval for breakthrough devices.	• We agree that there is a need for additional innovative regulatory pathways for devices.		• We are available to provide technical assistance (Roche Diagnostics).
Subtitle G – Expanded Access			
Sec. 1121. Expanded access policy as condition of expedited approval.			
Sec. 1122. Notification of			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
submitters of expanded access requests.			
Sec. 1123. GAO qualitative analysis on individual patient access to unapproved therapies and diagnostics.			
Sec. 1124. Expanded Access Task Force.			
Sec. 1125. Finalizing draft guidance on expanded access.			
Subtitle H – Facilitating Responsible Communication of Scientific and Medical Developments			
Sec. 1141. [to be supplied]			• We are available to provide technical assistance and encourage the Committee to actively explore opportunities to leverage work underway through the Harvard Multi-Regional Clinical Trial (MRCT) Center and TransCelerate BioPharma.
Subtitle I – Modernizing the Regulation of Social Media			
Sec. 1161. Dissemination of information about medical products using the Internet.	• We support the provisions of Sec. 1161, which would allow companies to provide safety & effectiveness information via a		• We are available to provide technical assistance.

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TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
	hyperlink in character-limited communications about a product via social media. Currently, we are limited in our ability to communicate about products via social media due to the need to include the full name of the product, as well as the safety information required by regulation. This language would allow for a significant broadening of the information that can be communicated by social media. • We support the timelines proposed by the Committee (*i.e.*, 12 months for draft regulation and guidance and subsequently six months for finalization).		
Subtitle J – Streamlined Data Review			
Sec. 1181. Streamlined data review program.	• We agree with the provisions in Sec. 1181 and appreciate the Committee's attention to the data review process for	• We believe that, rather than requiring the guidance document or the reports to Congress, it may be more	

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TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
	additional indications.	beneficial to have workshops to discuss and define the future use of data summaries in the application review process (this provision was originally discussed at the Friends of Cancer Research/Brookings Fall Meeting – and a follow up workshop and/or discussions on this topic would be less burdensome for FDA and perhaps more beneficial for stakeholders). Additionally, we believe it may be possible to implement this change with an internal CDER MAPP, which might be less burdensome to produce and clear than a guidance document. • We recognize that selection of additional indications may be dependent on prior indications for which a given therapy is approved and on the overall safety profile of the given	

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TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
		therapy. Taking the above under consideration, we propose that a transparent process for additional indications be defined, rather than creating a list of expanded indications.	
Subtitle K – Cures Acceleration Network			
Sec. 1201. Flexible research authority.			
Sec. 1202. Repurposing drugs.			
Subtitle L – Dormant Therapies			
Sec. 1221. Definitions.			
Sec. 1222. Capturing lost opportunities and creating new cures for patients.			
Sec. 1223. Implementation and effect.			
Subtitle M – New Therapeutic Entities			
Sec. 1241. Extended exclusivity period for certain new drug applications and abbreviated new drug applications.			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Subtitle N – Orphan Product Extensions Now			
Sec. 1261. Extension of exclusivity periods for a drug approved for a new indication for a rare disease or condition.	• We agree in concept with the need for additional incentives.		• We would like to work with the Committee to discuss incentives that would be the most meaningful to encourage additional drug development for rare diseases.
TITLE II – BUILDING THE FOUNDATION FOR 21ST CENTURY MEDICINE, INCLUDING HELPING YOUNG SCIENTISTS			
Subtitle A – 21st Century Cures Consortium Act			
Sec. 2001. Innovative Cures Consortium.			
Subtitle B – Medical Product Innovation Advisory Commission			
Sec. 2021. Medical Product Innovation Advisory Commission.			
Subtitle C – Regenerative Medicine			
Sec. 2041. Issuance of guidance on surrogate and intermediate endpoints for accelerated approval of regenerative medicine products.	• We agree that prospective evidentiary standards are essential for the efficient development and use of surrogate and intermediate	• We recommend that the Committee explore options to ensure that this work, while more defined in scope (limited to surrogate and intermediate	• We are available to support the Committee as they develop language that would facilitate the development of evidentiary standards for surrogate and

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TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
	clinical endpoints, by (1) providing sponsors with clarity and predictability, and (2) ensuring consistency in the Agency's approach.	clinical endpoints for Accelerated Approval of regenerative medicine products under 21 U.S.C. 356c), is coordinated with that described previously under Title I, Subtitle B, Sec. 1021 *Evidentiary Standards for the review of requests for the qualification of surrogate endpoints*.	intermediate clinical endpoints for Accelerated Approval of regenerative medicine products and to ensure that this work is synergistic with that outlined previously in Title I, Subtitle B, Sec. 1021.
Subtitle D – Genetically Targeted Platform Technologies for Rare Diseases			
Sec. 2051. Genetically targeted platform technologies for rare diseases.		• We request more information about the provisions in Sec. 2051.	• We would like to work with the Committee on these provisions (Roche Diagnostics).
Subtitle E – Sensible Oversight for Technology Which Advances Regulatory Efficiency			
Sec. 2061. Medical and health software defined.	• We agree in concept and appreciate the Committee's attention to medical and health software issues	• We believe more clarity on the use of the medical software in drug development is warranted.	• We would like to work with the Committee on these provisions (Roche Diagnostics).
Sec. 2062. Applicability and inapplicability of regulation.			• We would like to work with the Committee on these provisions.
Sec. 2063. Exclusion from definition of device.			• We would like to work with the Committee on these provisions.

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Subtitle F – Building a 21st Century Data Sharing Framework			
PART 1 – Improving Clinical Trial Data Opportunities for Patients			
Sec. 2081. Standardization of data in Clinical Trial Registry Data Bank on eligibility for clinical trials.			
Sec. 2082. Clinical Trial Data System.			
PART 2 – Improving Clinical Outcomes for Patients and Program Integrity Through CMS Data			
Sec. 2085. Expanding availability of Medicare data.			
Sec. 2086. Empowering patient research and better outcomes through CMS data.			
Sec. 2087. Allowing clinical data registries To comply with HIPAA privacy and security law in lieu of complying with the privacy and security provisions of the Common Rule.			
Sec. 2088. Access to CMS claims data for purposes of fraud analytics.			
PART 3 – Building a 21st Century Clinical Data Sharing System			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
<u>TITLE I</u> – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Sec. 2091. Commission on Data Sharing for Research and Development.			
Sec. 2092. Recommendations for development and use of clinical data registries.	• We agree with the proposed list of recommendations for development and use of clinical data registries.	• We believe that data from clinical registries could be utilized as virtual controls for future clinical trials, so allocating more funds and resources to develop methods/processes in support of this utilization is warranted.	
Subtitle G – Utilizing Real-World Evidence			
Sec. 2101. Utilizing real-World evidence.	• We appreciate the Committee's proposal on the utilization of real world evidence to advance drug development (support of new indications or post-approval commitments).	• We believe that more resources towards new methods development are warranted and would advance the utilization of real world evidence.	
Subtitle H – Coverage with Evidence Development			
Sec. 2121. Authority for coverage with evidence development for medical de- vices under the Medicare program.			

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<u>TITLE I</u> – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Subtitle I – Combination Products			
Sec. 2141. Regulation of combination products by the Food and Drug Administration.	• We agree that there are issues with respect to Combination Products that require attention. The regulation of In Vitro Diagnostic Products for Targeted Therapies (CDx) is working well, and lessons learned from resolving CDx challenges could be used to develop changes needed for greater efficiency with respect to the regulation of Combination Products. Guidance Documents, Internal Procedures, workshops and publications were used to better define and delineate regulatory pathways for CDx products. Development of regulatory pathways for CDx products has resulted in very effective interactions between CDRH and CDER, and this should be possible for Combination Products. Particularly useful are	• While a GAO report documenting performance might be useful, we believe resources might be better spent on the development of internal MAPPs and guidance toward correcting operational issues and challenges of coordination with respect to Combination Products.	• We are available to provide assistance to the Committee in terms of what has helped to deal with past challenges of CDx and coordination issues between CDRH and CDER, which have been resolved (Roche Diagnostics).

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TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
	provisions noting that there should be a single Center as a sole point of contact that coordinates with the consulting Center and that the communications from that Center are binding.		
Sec. 2142. GAO report on FDA regulation of combination products.			
Subtitle J – Modernizing Regulation of Diagnostics			
Sec. 2161. [to be supplied].			
Subtitle K – Interoperability			
Sec. 2181. [to be supplied].			
Subtitle L – NIH-Federal Data Sharing			
Sec. 2201. Sharing of data generated through NIH-funded research.			
Subtitle M – Accessing, Sharing, and Using Health Data for Research Purposes			
Sec. 2221 Accessing, sharing, and using health data for research			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
purposes.			
Subtitle N –21st Century Chronic Disease Initiative Act			
Sec. 2241. Plan for longitudinal study on outcomes of patients with a chronic disease.			
Subtitle O – Helping Young Emerging Scientists			
Sec. 2261. Funding research by emerging scientists through Common Fund.			
Sec. 2262. Report on trends in age of recipients of NIH-funded major research grants.			
Subtitle P – Fostering High-Risk, High-Reward Science			
Sec. 2281. High-risk, high-reward research program.			
Subtitle Q – Precision Medicine			
Sec. 2301. [to be supplied].			
TITLE III – MODERNIZING CLINICAL TRIALS			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Subtitle A – Clinical Research Modernization			
Sec. 3001. Protection of human subjects in research; applicability of rules.			
Sec. 3002. Use of institutional review boards for review of investigational device exemptions.			
Subtitle B – Broader Application of Bayesian Statistics and Adaptive Trial Designs			
Sec. 3021. Clinical trial modernization.	• We appreciate the committee's attention to alternative statistical methods. • We agree that a broader use of adaptive study designs would benefit drug development.	• We believe that more resources and funds are needed to investigate new methods in order to gain a better understanding of benefits/ challenges associated with utilization of these methods.	
Subtitle C – Postapproval Studies and Clinical Trials			
Sec. 3031. Evaluations of required postapproval studies and clinical trials.			
Subtitle D – Pediatric Research Network Improvement			
Sec. 3041. National Pediatric	• We agree in concept with the		• We are available to provide

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Research Network.	provisions outlined in Sec. 3041.		technical assistance on pediatric matters relating to the Bill.
Subtitle E – Global Pediatric Clinical Trial			
Sec. 3061. Sense of Congress.	• We agree in concept with the provisions outlined in Sec. 3061.		• We are available to provide technical assistance on pediatric matters relating to the Bill.
TITLE IV – ACCELERATING THE DISCOVERY, DEVELOPMENT, AND DELIVERY CYCLE AND CONTINUING 21ST CENTURY INNOVATION AT NIH, FDA, CDC, AND CMS			
Subtitle A – National Institutes of Health			
Sec. 4001. NIH research strategic investment plan.			
Sec. 4002. Biomedical research working group to reduce administrative burden on researchers.			
Sec. 4003. NIH Travel.			
Sec. 4004. Increasing accountability at the National Institutes of Health.			
Sec. 4005. GAO report on Common Fund.			
Sec. 4006. Exemption for the			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
National Institutes of Health from the Paper-work Reduction Act requirements.			
Sec. 4007. Additional funding for NIH Common Fund.			
Sec. 4008. Additional funding for NIH brain research.			
Sec. 4009. NCATS Phase IIB Restriction.			
Subtitle B – Advancing Research for Neurological Diseases			
Sec. 4021. National neurological diseases surveillance system.			
Subtitle C – Vaccine Access, Certainty, and Innovation			
PART 1 – Development, Licensure, and Recommendations			
Sec. 4041. Prompt review of vaccines by the Advisory Committee on Immunization Practices.			
Sec. 4042. Review of transparency and consistency of ACIP recommendation process.			
Sec. 4043. Guidance on vaccine development.			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Sec. 4044. Meetings between CDC and vaccine developers.			
Sec. 4045. Modifications to priority review voucher program for tropical diseases.			
Sec. 4046. Guidance on changes to an approved application for biological products.			
Sec. 4047. Expediting the process for export certifications for vaccines.			
Sec. 4048. NIH vaccine research.			
PART 2 – Medicare, Medicaid, and Other Provisions			
Sec. 4061. Requiring prompt updates to Medicare program upon issuance of ACIP recommendations.			
Sec. 4062. Encouraging health plans to establish programs to increase adult immunization.			
Subtitle D – Reagan-Udall Improvements Bill			
Sec. 4081. Reagan-Udall Foundation for the Food and Drug Administration.			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Subtitle E – FDA Hiring, Travel, and Training			
Sec. 4101. [to be supplied].			
Subtitle F – FDA Succession Planning			
Sec. 4121. Professional development of FDA staff.			
Sec. 4122. FDA management succession planning.			
Subtitle G – Disposable Medical Technology			
Sec. 4141. Coverage of certain disposable medical technologies under the Medicare program.			
Subtitle H – Local and National Coverage Decision Reforms			
Sec. 4161. Improvements in the Medicare local coverage determination (LCD) process.			
Subtitle I – Telemedicine			
Sec. 4181. Advancing telehealth opportunities in Medicare.			
Subtitle J – Revise IPPS New Technology Add-On Payment (NTAP)			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Sec. 4201. Coding and reimbursement reforms.			
Subtitle K – Lowering Medicare Patients OOP Costs			
Sec. 4221. Medicare site-of-service price transparency.			
Subtitle L – Global Surgery Services Rule			
Sec. 4241. Treatment of global surgery services rule.			
Subtitle M – Providers Consolidation and Medicare Payments Examined Through Evaluation			
Sec. 4261. Rulemaking that implements certain Medicare payment changes to consider effects on provider consolidation.			
Subtitle N – Medicare Part D Patient Safety and Drug Abuse Prevention			
Sec. 4281. Establishing PDP safety program to prevent fraud and abuse in Medicare presciption			
Sec. 4282. Part D suspension of claims payment.			
Sec. 4283. Improving activities of Medicare Drug Integrity			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Contractors (MEDICs).			
Sec. 4284 Requiring e-prescribing for coverage of covered part D controlled substances.			
Subtitle O – Accelerating Innovation in Medicine			
Sec. 4301. Establishment of manufacturer opt-out program for medical devices.			
Subtitle P – Medicare Pharmaceutical and Technology Ombudsman			
Sec. 4321. Medicare pharmaceutical and technology ombudsman.			
Subtitle Q – Ensuring Local Medicare Administrative Contractors Evaluate Data Related to Category III Codes			
Sec. 4341. Ensure local Medicare administrative contractors evaluate data related to Category III codes.			
Subtitle R – Advancing Care for Exceptional Kids			
Sec. 4361. Findings.			
Sec. 4362. Establishment of Medicaid and CHIP Care			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Coordination program for children with medically complex conditions as Medicaid State option.			
Subtitle S – Continuing Medical Education Sunshine Exemption			
Sec. 4381. Exempting from manufacturer transparency reporting certain transfers used for educational purposes.			
Subtitle T – Medical Testing Availability			
Sec. 4401. Clarification regarding research use only products.	• We agree in concept with clarifications.	• We disagree with sunset provisions.	• We are available to provide technical assistance with respect to provisions, and sunset provisions, which we believe should be eliminated (Roche Diagnostics).
TITLE V – ACCELERATING THE DISCOVERY, DEVELOPMENT, AND DELIVERY CYCLE AND CONTINUING 21ST CENTURY INNOVATION AT NIH, FDA, CDC, AND CMS			
Subtitle A – Manufacturing Incentives			
Sec. 5001. Extension of exclusivity period for American-manufactured			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
generic drugs and biosimilars.			
Subtitle B – 21st Century Manufacturing			
Sec. 5021. Updating regulations and guidance on current good manufacturing practice requirements.			
Subtitle C – Controlled Substances Manufacturing and Exports			
Sec. 5041. Re-exportation among members of the European Economic Area.			
Subtitle D – Medical Device Reforms			
Sec. 5061. Third-party quality system assessment.	• We agree in concept with the provisions outlined in Sec. 5061.		• We are available to provide technical assistance (Roche Diagnostics).
Sec. 5062. Valid scientific evidence.	• We agree in concept with the provisions outlined in Sec. 5062.		• We are available to provide technical assistance (Roche Diagnostics).
Sec. 5063. Training and oversight in least burdensome means concept.	• We agree in concept with the provisions outlined in Sec. 5063.		• We are available to provide technical assistance (Roche Diagnostics).
Sec. 5064. Recognition of standards.	• We agree in concept with the provisions outlined in Sec. 5064.		• We are available to provide technical assistance (Roche

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Subtitle A – Patient-Focused Drug Development			
			Diagnostics).
Sec. 5065. Notification of marketing of certain class I devices.	• We agree in concept with the provisions outlined in Sec. 5065.		• We are available to provide technical assistance (Roche Diagnostics).
Sec. 5066. General and specific uses.	• We agree in concept with the provisions outlined in Sec. 5066.		• We are available to provide technical assistance (Roche Diagnostics).
Sec. 5067. Humanitarian device exemption application to in vitro diagnostics.	• We agree that the provisions need to be changed.		• We are available to provide technical assistance (Roche Diagnostics).
Sec. 5068. Advisory committee process.			
Subtitle E – Supply Chain Security for Devices			
Sec. 5081. Short title.			
Sec. 5082. Device distribution supply chain.			
Sec. 5083. Authorized trading partners.			
Sec. 5084. National licensing standards for wholesale device distributors.			
Sec. 5085. National licensing standards for third-party logistics providers.			

Section/Topic	Areas of Agreement	Areas of Concern	Areas to Provide Technical Assistance
TITLE I – PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS			
Subtitle A – Patient-Focused Drug Development			
Sec. 5086. Waivers and exemptions.			
Sec. 5087. Uniform national policy.			
Sec. 5088. Penalties.			

SUMMARY

Priority provisions for comment:

- **Title II, Subtitle H. Sec 2121 –** Coverage with Evidence Development – Support narrowing CED to devices only. Modify to explicitly exclude drugs and biologics from CED; rescind previous CED guidance documents; re-title new guidance to signal narrowed
- **Title IV, Subtitle Sec. Sec. 4201(b).** Replacing NDC Codes with HCPCS Codes under Medicare Part B. Oppose due to directional rebate exposure; operational concerns; technical limitations of NDC.

Priority provisions to add:

- Incentivizing Innovation in Alternative Payment Models (CONSIDER TITLE II)
- Correct Flawed Methodologies to Measure Quality and Cost (CONSIDER TITLE II)
- Additional protections—CMMI demonstrations and pilot programs (CONSIDER TITLE II)
- Strengthen Clinical Trial Coverage (CONSIDER TITLE II)

COMMENTS ON DRAFT

TITLE I—PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND AD- DRESSING UNMET NEEDS

Subtitle D—Antibiotic Drug Development

Sec. 1061. Approval of certain drugs for use in a limited population of patients.

Sec. 1062. Susceptibility test interpretive criteria for microbial organisms.

Sec. 1063. Election to convey a portion of extended exclusivity period applicable to qualified infectious disease products.

Sec. 1064. Encouraging the development and use of new antimicrobial drugs.

GNE Position: Support.

- *Ensuring adequate hospital reimbursement of new antimicrobial drugs will encourage development of new classes of antimicrobial drugs by supporting a commercial marketplace. Genentech believes that in order for this provision to be the most supportive of antibiotic development that this provision should not be budget neutral and that the additional payments should not come from existing hospital inpatient payments.*
- *Genentech also seeks to update the GAIN Act to extend the additional five-year exclusivity for Qualified Infectious Disease Products (QIDPs) to biologics and large molecules*

Subtitle G – Expanded Access

Genentech supports the goals of an expanded access program but believes there could be greater clarification as to what the programs should or should not address. Additionally, as a company that currently has an active expanded access policy, we appreciate the opportunity to share how our specific program is currently run. One question is should there be an overarching policy or a molecule-specific policy/approach? The latter would be challenging to meet for many companies. At Genentech, we have a single point of contact, procedures and general criteria in place. The time frame is somewhat variable and often determined by the responsiveness of the physician and whether or not a molecule-specific plan is already in place at the time of the request.

Regarding the Covered Investigational Drug Section—it is important to note that many desired drugs do not have breakthrough or fast track status. There could be greater clarification as to whether or not the draft language requires that molecules that meet one of these three criteria must be made available through Compassionate Use/Expanded Access Policy or is it a trigger that would make the company have to once and for all describe their company policy? For example, suppose a company was granted breakthrough status on a molecule this week—is the language stipulating that it would be that designation that triggers the company to have to comply wit the rest of the requirements?

Genentech currently has a policy of notification of submitters of request and supports its inclusion in legislation. Additionally, we believe that the timeframes laid out in the draft document are reasonable. One question on qualitative analysis is whether the intent is to look at the molecule as a whole or specific disease where the molecule is being studied. For example, there might be a pediatric request for Product X in a teenager with lymphoma but the company only has data on the molecule in older populations, which served as the basis for the submission. What standard is being considered—the molecule or the molecule plus the indication?

Genentech supports the composition of the task force piece. The duties of the task force could benefit from a more specific definition of "comparable of satisfactory alternative therapy available." One suggestion is to specify in the third subsection of the task force duties to look at aggregate data on all individual patient use to identify any trends and patterns that could inform future research. Lastly, it should be noted that in the task force duties subsection six, the cost would be difficult to calculate and will vary dramatically from company to company based on manufacturing and human resources currently in place.

Subtitle H – Facilitating Responsible Communication of Scientific and Medical Developments

Genentech is very supportive of the Committee's intent to include a proposal that will update FDA's current rules and policies governing what manufacturers may communicate around uses of their own products. We fully support the need for important protections to ensure that this information is truthful and non-misleading, but that should not limit the ability of providers, payers and patients to obtain access to a robust body of evidence that will allow them to make the most appropriate clinical decisions. Advancements in the ability of entities and individuals to analyze and use data have become an integral part of our 21st century healthcare system. It is critical to have a regulatory framework that reflects this new reality. We appreciate the time already spent by the Committee with us to discuss this issue and we hope to continue this engagement around the proposal we submitted or some other variation.

TITLE II—BUILDING THE FOUNDATION FOR 21ST CENTURY MEDICINE, INCLUDING HELPING YOUNG SCIENTISTS

Subtitle A: 21st Century Cures Consortium Act

Sec. 2001 (p. 131) Create public-private partnership to accelerate innovative cures [Board of Directors would consist of 22 Directors: 5 Directors designated from NIH, FDA, and CMS; 8 Directors from the biopharmaceutical and medical device industry appointed by the Government Accountability Office (GAO); and 9 Directors representing academic researchers, patients, health care providers, and insurers, appointed by GAO.]

Subtitle B. Medical Product Innovation Advisory Commission

Sec. 2021. Creation of Medical Product Innovation Advisory Commission to study Federal policies from NIH, FDA, and CMS that impact the discovery, development, and delivery of medical products, as well as the interaction of those policies and steps that could be taken to accelerate the cycle. The Commission would be required to submit two reports to Congress each year that include recommendations for policies to accelerate the discovery, development, and delivery cycles. Would consist of 17 Commissioners appointed by GAO—with representatives from academic research, practitioners in the healthcare system, patients, payors, and experts from industry.

GNE Position: Support with modification.

- *Although Genentech supports FDA and CMS– among other stakeholders, working together to promote and accelerate the development and delivery of innovative therapies to patients, we ask that the Committee recognize that the unique missions of these two agencies remain distinct and not be comingled or compromised.*
- *Congress deliberately bestowed FDA and CMS with distinct authorities and standards for approval and coverage decisions respectively, consistent with the different missions and constituencies of the agencies. FDA has the appropriate combination of expertise and resources to review and approve study design and results of clinical trials needed to demonstrate that drugs and biologics are safe and effective. As part of the Consortium mandate, CMS should not attempt to use its limited resources to duplicate this mandate.*
- *Consider modifying sections 2001 and 2021 and specific aspects of their mandates (for example, those related to integrating "steps" in the innovation cycle.)Recommend modifying to make clear that decisions about coverage, coding and reimbursement should occur separate and apart from Consortium & Commission.*

Subtitle F—Building a 21st Century Data Sharing Framework

PART 2—IMPROVING CLINICAL OUTCOMES FOR PATIENTS AND PROGRAM INTEGRITY THROUGH CMS DATA

Sec. 2085. (p. 168) Expanding availability of Medicare data. [Expands availability of Medicare data for evaluation of new care models, quality improvement activities and other patient care activities.

Sec. 2086. (p.180) Empowering patient research and better outcomes through CMS data. [Allows a state or qualified researcher (without regard to entity's commercial/institutional affiliation) to have access to CMS research files, including Part D data.]

Sec. 2088. (p. 184) Access to CMS claims data for purposes of fraud analytics. [Allows expanded data access by third parties for purposes of fraud prevention.]

GNE position: Support with suggestions to strengthen.

- *Genentech supports efforts to expand use of Medicare data to improve healthcare quality.*

- *Data releases should occur in a timely manner to allow for actionable and meaningful decision-making. At the same time, timeliness must be balanced with quality control practices to ensure that data is accurate.*
- *In order to prevent misinterpretation by researchers and others, datasets should include complete documentation – such as descriptions of limitations of the data.*
- *Claims data available should not be limited to Medicare Parts A & B. Claims data for Medicare Advantage, Part D, and Medicaid should be made widely available as well.*

PART 3—BUILDING A 21ST CENTURY CLINICAL DATA SHARING SYSTEM

Sec. 2092. (p. 190) Recommendations for development and use of clinical data registries. [Secretary shall make recommendations for the development and use of registries integrated with practice guidelines, and best practices or standards of care.]

GNE position: Support with modification.

- *While Genentech supports efforts to maximize the use of real-world data to inform and improve patient care, we also recognize that clinical guidelines are based on the average patient, and therefore are not and cannot be appropriate in every instance. We urge the Committee to ensure that recommendations do not discourage individualized patient care and allow for integration of new and innovative therapies into practice.*

- *Recommend adding language which further clarifies the intent and use of integrated guidelines:*
    - *Integrated practice guidelines should be used solely to improve clinical decisionmaking and patient care and should not be used as a cost-control mechanism; should not be used to restrict patient access to therapies; and should not interfere with physician decision-making.*
    - *Integrated practice guidelines should not be used to determine coverage and payment*
- *Development of integrated guidelines should go through a public and transparent process with opportunity for stakeholder engagement.*
- *Initiative should be used to reduce inappropriate variation but not to prevent appropriate variation*

Subtitle G: Utilizing Real-World Evidence

Sec. 4141. Coverage of Certain Disposable Medical Technologies under the Medicare Program. Sec. shall est. a single payment amount for what is otherwise DME but is not "durable"

GNE Position: Support with modifications to strengthen

- *Allow the substitution of more advanced disposables (such as nebulizers) for DME technologies that are class 2 devices.*

Subtitle H—Coverage with Evidence Development

Section 2121. Authority for coverage with evidence development for medical devices under the Medicare program. [Codifies CED for all items and services.] Draft would amend the Social Security Act to provide an exception to the "reasonably and necessary services" requirement established under section 1862(a)(1)(A) of the Social Security Act for Medicare coverage of "CED items or services." CED items or services are defined as items or services that are for coverage with evidence

development, which in turn is defined as items or services where: (1) the item or service is furnished to individuals as part of a clinical study performed to determine whether the item or service improves the health outcomes of individuals, and (2) the furnishing of the item or service determined by CMS to be reasonable and necessary to the carrying the clinical study.

GNE Position: Oppose codifying CED for all items and services; support limiting CED to medical devices under the Medicare program. (PRIORITY)

- *Genentech has long maintained that CED is not appropriate for FDA-approved and medically accepted uses of drugs and biologics – that is, off-label uses of drugs and biologics supported in certain compendia and peer-reviewed journals.*
- *Provision should be modified to exclude all drugs and biologics from CED (ie. authority for CED should not be codified for drugs and biologics). Additionally, existing CED guidance (finalized November 20, 2014) should be withdrawn and replaced with new guidance with narrowed scope. Title of new guidance should reflect this narrowed scope.*

TITLE IV—ACCELERATING THE DISCOVERY, DEVELOPMENT, AND DELIVERY CYCLE AND CONTINUING 21ST CENTURY INNOVATION AT NIH, FDA, CDC, AND CMS

Subtitle H—Local and National Coverage Decision Reforms

Sec. 4161. (p. 286) Improvements in the Medicare local coverage determination (LCD) process.[Requires each Medicare administrative contractor (MAC) to create a process for development of LCD that includes public comment periods, meetings and disclosure of decisional information.]

***GNE Position**: Support.*

- *Genentech believes that this proposal would strengthen local coverage determination (LCD) process increase transparency and consistency in local coverage process, specifically by helping to ensure that stakeholders both (1) know about proposed LCDs; and (2) have ample opportunity to work with clinicians and other scientific and technical experts to develop comments on those proposed LCDs.*
- *CMS needs to ensure there are minimum standards in place to prevent a more complex landscape with 10 completely different processes.*

Subtitle I—Telemedicine

Sec. 4181. (p. 291) Advancing telehealth opportunities in Medicare. [Creates and expands coverage and payment for telehealth services.]

GNE Position: Support.

- *Genentech recognizes that telemedicine has the ability to improve efficiency and help overcome health delivery problems such as improving patient access to medical specialists.*
- *Evidence has shown significant benefit of telemedicine to effectively diagnose and treat patients suffering from a stroke. We believe that expanding Medicare coverage of telestroke services to geographical regions outside of rural areas (such as urban an suburban areas) would have significant benefit on outcomes of Medicare beneficiaries*

Subtitle J—Revise IPPS New Technology Add-On Payment (NTAP) Reimbursement Amounts

Sec. 4201 Coding and Reimbursement Reforms

Sec. 4201 (a) (p. 299) Coding and reimbursement reforms. [Creates an appeals process for NTAP through administrative law judge (ALJ) process.]

GNE Position: Support with modifications to strengthen.

- *Genentech supports the need to increase transparency in the NTAP decision-making process.*
- *Consider redefining the criteria against which a product is granted NTAP and the NTAP payment level.*
- *Specifically, consider redefining the newness criteria for an NTAP[1] to refer to the date of approval for each indication rather than the date of the first approved indication. This is especially important for drugs and biologics targeting rare diseases to ensure that patients, for whom other treatments are often nonexistent, are able to access these therapies as soon as they reach the market and to ensure the preservation of incentives to develop therapies in this space.*

Sec. 4201(b). Proposes to replace Level II HCPCS codes with NDC codes for the purposes of Medicare Part B coding.

GNE position: Oppose (PRIORITY)

Genentech recognizes and supports the need to modernize the coding system and appreciates the Committee's attention to this issue, however, we cannot support for the following reasons:

- *Potential for Part B rebate exposure.*
  - *Unsure of all implications, but directionally would increase exposure.*

- *Some may argue that the NDC makes it easier to trace the drug to the manufacturer.*
  - *Identifies the drug but not the manufacturer.*

- *However a there are technical limitations to using an NDC. It requires a "second step" of cross walking the HCPCS to the NDC is required, which is why it is operationally more difficult to apply rebates to physician-administered drugs.*
  - *HCPCS codes account for multi-use packaging whereas NDCs do not*
  - *NDCs are in sales/packaging units, whereas dosing may be some multiple or portion of the package size.*
  - *HCPCS don't have this problem because their unit of measure is based on the lowest common denominator of all NDCs in the code)*

- *Significant operational burdens imposed on our customers.*
  - *In addition to facing reporting requirements under various quality programs like VBM, PQRS and meaningful use, they are facing the transition to ICD-10 at the end of year.*
  - *Switching to NDC will require significant system changes to support claim submission. There is a history here -- hospitals sued over requirement to report NDCs because of this burden.*

Subtitle K—Lowering Medicare Patients OOP Costs

Sec. 4221. (p.304) Medicare site-of-service price transparency. [The Director of the National Institute for Standards and Technology (NIST) will work with HHS to create a searchable website that allows Part A and Part B Medicare beneficiaries to compare the rate of payment and the maximum out-of-

[1] 42 C.F.R. 412.87(b).

pocket costs for various items and services furnished by different providers in different settings within a payment area or MA plan. The Director would be required to assess the feasibility of using real-time claims data from CMS to determine the extent to which a beneficiary searching for an item or service is subject to a deductible or out-of-pocket cost limitation.]

GNE Position: More information needed.

- *Genentech supports the need to improve transparency in out-of-pocket costs.*
- *More information is needed as proposal may have significant logistical and operational challenges given the diversity of geographical locations and entity types in which services are provided and the reimbursement structure of different parts of the Medicare program (e.g., Medicare Part C—Medicare Advantage—doesn't reimburse for individual services but provides plans with a per-enrollee reimbursement based on annual plan bids).*
- *Also, more information needed to ensure protection of proprietary information.*

Subtitle M—Providers Consolidation and Medicare Payments Examined Through Evaluation

Sec. 4261. (p. 307) Rulemaking that implements certain Medicare payment changes to consider effects on provider consolidation. Secretary must review how proposals will impact provider consolidation.

GNE Position: Support with suggestions to strengthen.

- *Genentech supports the need to understand existing and identify trends in provider consolidation, especially the acquisition of independent provider practices by large hospitals/hospital systems.*
- *In addition to reviewing Medicare payment proposals to assess impact on provider consolidation, Secretary should also include an assessment of whether the proposal would lead to greater out-of-pocket spending for Medicare beneficiaries.*

Subtitle P—Medicare Pharmaceutical and Technology Ombudsman

Sec. 4321. (p. 322) Medicare Pharmaceutical and Technology Ombudsman. [Creates an ombudsman within CMS with the role of receiving medical technology developers' complaints on coding, coverage and reimbursement and issue an annual report to Congress]

GNE Position: Support with suggestions to strengthen.

- *Ensure that proprietary data is excluded from any information made public*

IDENTIFIED GAPS/PROPOSALS FOR CONSIDERATION

1. ***Incentivizing Innovation in Alternative Payment Models. (CONSIDER TITLE II)***
   Rationale:
   Genentech believes that alternative payment methodologies and delivery of care models have great potential to achieve the "triple aim" of higher quality care for individuals, better health for populations, and lower per capita costs. We also believe that these goals must – and can – be structured to adapt to new emerging technologies and cures while still incentivizing the development of cures. For instance, if improperly designed, APMs risk incentivizing the underutilization of care and, if they mainly focus on cost-containment, can limit patient access

to innovative therapies. Therefore, CMS should be required to examine and identify mechanisms within APMs that account for the emergence of new technologies and the evolution of medicine and science.

Proposals:

- *Implement "pass-through" process for 2-3 years to allow separate payment for certain new drugs and biologics (similar to pass-through payment in hospital outpatient setting).*
- *Require CMMI to commission study to examine how to address payment for innovative technologies/personalized medicines in the context of alternative payment models.*

2. ***Correct Flawed Methodologies to Measure Quality and Cost (CONSIDER TITLE II)***

Rationale:

Current cost and quality measurement approaches do not adequately support personalized, patient-centered care. Rather, they can actually undermine patient access to the most clinically appropriate treatment and penalize physicians. Additionally, current coding systems may not accurately capture the severity of disease – such as cancer— which can unduly penalize physicians and patients in the form of inaccurate risk adjustment formulas and overall payments

Proposals:

- *Budgetary Timelines: Guardrails against decisions that are primarily based on short-term financial gains at the expense of long-term health*
- *Timely access to data: Reduce lag time associated with reporting cost and quality measures*
- *Understanding adequacy of coding systems to identify staging in metastatic cancers. Conduct study to understand the limitations of current and future coding systems (e.g., ICD-10-CM) in capturing severity of disease and staging information. Until such study has been conducted and findings disseminated, metastatic cancers should be excluded from*
- *Streamline the measures/reporting processes – implement more standardized process across the different quality initiatives*

3. ***Additional protections—CMMI demonstrations and pilot programs (CONSIDER TITLE II)***

Rationale:

Incorporation of stakeholder input in design and implementation of demonstration project: CMS (the secretary) should consult stakeholders—including patients, providers, and the biopharmaceutical industry—when designing and implementing the demonstration project.

Proposals:

CMS should use notice and comment periods, open door forums or other mechanisms to seek input from interested parties. Meaningful incorporation of public comment will limit unintended consequences of the demonstration's design.

Expansion of demonstration project: Any expansion of the demonstration project, including duration and scope of the model, should take into account the evaluation report and be subject to rulemaking

4. ***Strengthen Clinical Trial Coverage (CONSIDER TITLE II)***

Rationale:

- *Section 2709 of ACA establishes a federal minimum requirement for coverage of items and services related to clinical trials. However, clarity and improvements are needed for it to be meaningful to patients. Without additional guidance, implementation will continue to be inconsistent throughout the country.*

Proposals:

- *Ensure that the prevention, detection, and treatment of complications arising from clinical trials are covered by group health plans and insurance issuers as routine patient costs. For example, to ensure consistency, the terms "standard of care costs", "usual care costs" and "routine care costs" should be abandoned and replaced with any test, procedure, medicine, or other intervention that is for "the direct clinical management of the patient" or that is*

"reasonable and medically necessary" to ensure safety. Create geographic safeguards to ensure patients can access in-network providers

- *Prevent group health plans and insurance issuers from requiring patients to travel extensive distances to enroll in a clinical trial with an in-network provider*
- *Ensure patients are informed in an unambiguous manner as to whether or not their group health plan or insurance issuer covers the routine costs associated with participation in clinical trials*

Generic Pharmaceutical Association

Generic Pharmaceutical Association Comments on the "21st Century Cures Act"

The Generic Pharmaceutical Association (GPhA) appreciates the opportunity to provide our initial written comments on the recently released 21st Century Cures discussion document. GPhA believes that the earlier new treatments can be approved, the earlier patients can access new generic medicines. The competition in the pharmaceutical marketplace currently provided by generic drugs – and the competition that will soon be provided by biosimilars – is an important part of the cycle of new drugs and is vital in both assuring patient access to life-saving cures and in spurring innovation and research into new cures, both brand and generic. Our goal is for the final 21st Century Cures document to reflect the important role of generic competition in spurring innovation and ensuring access to affordable medicines. The following comments address preliminary ways that we believe that draft could better balance incentives for innovation and encouraging competition.

We strongly support the 21st Century Cures initiative's goal of accelerating the discovery, development, and delivery of promising new drugs to patients in the United States. We commend Chairman Upton and Congresswoman DeGette for their tireless work toward achieving this important goal, and we look forward to continuing to work with you and your staff to ensure that our nation's policies support this goal. Our member companies are carefully reviewing the complete document, and we want to give your thoughtful proposals the consideration they deserve. We have included below our preliminary comments. We anticipate there will be additional comments on other important provisions after our membership has had an opportunity to complete its review, keeping in mind GPhA's mission to improve the lives of patients by providing timely access to affordable medicines. We look forward to working with the Committee as this process moves forward.

GPhA respectfully requests that the Committee consider the inclusion of a proposal addressing abuse of an FDA safety program as a means to delay generic entry. In the 113th Congress, Rep. Steve Stivers and Rep. Peter Welch introduced the FAST Generics Act (H.R. 5657), which would close this loophole and prohibit companies adopting restricted access practices solely as a strategy to avoid generic competition.

The Food and Drug Administration Amendments Act of 2007 (FDAAA) gave FDA the authority to require a Risk Evaluation and Mitigation Strategy (REMS) to ensure that the benefits of a drug or biological product outweigh its risks. Certain drug manufacturers have been using tactics that initially grew out of REMS Elements To Assure Safe Use (ETASU) requirements to delay generic competition for REMS and non-REMS products alike. Specifically, manufacturers are employing restricted distribution networks to deny manufacturers of generics and biosimilars access to product samples they need to obtain FDA approval and market entry. Companies are also developing additional ways to abuse REMS programs to prevent and delay generic competition.

The abuses are growing, and the resulting delay in generic and biosimilar competition is negatively affecting patient access to life-saving medicines. Both the FDA and the Federal Trade

Commission (FTC) have taken steps to ameliorate abuses with very limited success, and legislation is needed to close this loophole that is inhibiting generic manufacturer research into new generics and biosimilars and delaying patient access to life-saving, affordable cures. According to a recent study, the ongoing abuse of the programs is costing the American health care system and patients $5.4 billion in annual pharmaceutical spending that could be saved if the 40 drugs examined were allowed to come to market. The federal government bears a third of this burden, or $1.8 billion.

In addition to addressing REMS abuse, there are other recommendations that are currently being considered by our membership. We look forward to sharing our thoughts on positive reforms to spur cost savings through competition and advance broader patient access to high-quality medicines.

Antibiotic Drug Development (Subtitle D)

GPhA supports the goal of incentivizing the development of new antibiotics, and we applaud the inclusion in the discussion document of the bipartisan ADAPT Act (section 1061-1062). This provision takes a targeted approach to incentivizing the development of antibiotics by promoting greater collaboration between FDA and industry.

We are concerned, however, with Section 1063 of the discussion draft, which would establish "wildcard exclusivity" for developers of antibiotics using the GAIN Act Qualified Infectious Disease Product (QIDP) designation. The GAIN Act pathway has only been in effect for a little more than two years, and there have been immediate positive results with greater development and approval of new antibiotics. Provisions of the ADAPT Act are a more targeted and effective approach to encourage the development of new antibiotics and are a helpful addition to the GAIN Act. It is premature to add additional exclusivity on top of the GAIN Act after only two years. While GPhA supports the goal of spurring the development of new antibiotics, this legislative proposal could have unintended consequences.

Manufacturers receiving the QIDP designation already receive expedited approval and five years of additional market exclusivity – for a total of ten years of market exclusivity. As of September 2014, FDA had granted the QIDP designation to 39 antibiotics under development and approved three. Under a "wildcard exclusivity" regime this could lead to 468 months of additional exclusivity on blockbuster brand products that could delay patient access to more affordable versions of these life-saving medicines

A twelve-month wild-card exclusivity extension delaying generic or biosimilar entry could have significant implications for healthcare spending, including by Medicare, Medicaid, and the VA – and would delay patient access to the more affordable versions of the drug. For example, in 2010 U.S. sales of the blockbuster cholesterol drug Lipitor were $5.3 billion. In 2013, U.S. sales of the biologic Herceptin used to treat breast cancer were $1.6 billion.

Dormant Therapies (Subtitle L)

GPhA supports the goal of promoting the development of therapies for complex diseases. The Dormant Therapies language as currently drafted, however, raises questions regarding the definitions of key concepts and the interaction with the current processes under the Hatch-Waxman Act relating to Abbreviated New Drug Applications (ANDAs). As this proposal would grant 15 years of regulatory protection to "dormant therapies," which is three times the five years for new chemical entities, more than twice the seven years for orphan drugs and more than currently exists for biologics, GPhA believes this proposal raises serious concerns. The expansive definition of dormant therapies would sweep in drugs that would have been developed even without the special incentives or that have only marginal improvements over currently marketed drugs. Further refinement of the definition to more truly reflect their goals should be undertaken by the sponsors of the legislation.

As drafted there is too much uncertainty around generic and biosimilar market entry. Instead of establishing a predictable timeline for the market entry of generic drug and biosimilar products, the section would create a host of questions regarding generic drug and biosimilar applications, including the effect on first applicants' rights to the 180-day exclusivity period. It also creates questions around potential patent term extensions for changes made during the extended exclusivity period blocking generic entry in perpetuity.

While perhaps unintentional, evergreening is facilitated by this provision (a practice whereby manufacturers are able to make relatively minor changes to their products to provision would extend patent protections for dormant therapies beyond the end of their 15-year exclusivity periods). It appears as currently drafted that this provision would provide for patent term extensions for all uses of a product and is not limited to the dormant indication. Further, by delaying generic competition, the MODDERN Cures Act – the House version of the bill – would have increased spending by **$121 billion** on 117 drugs between 2001 and 2010, according to recent Congressional testimony.[i] GPhA would like to continue to discuss with the Committee the specific questions raised by the draft in this regard.

Extension of Exclusivity Period for American-Manufactured Generic Drugs and Biosimilars (Section 5051)

GPhA appreciates the efforts of Health Subcommittee Vice Chair Guthrie in drafting this section of the discussion document and supports the goal of encouraging investment in American manufacturing. The U.S. generic industry is a growing and vibrant industry, and GPhA member companies currently employ more than 62,000 people in thirty-three states. This approach raises several questions that will need to be addressed before the Association can take a position. Among those are the sourcing of Active Pharmaceutical Ingredient (API) and excipients, potential trade implications concerning the North American Free Trade Agreement (NAFTA) or the General Agreement on Tariffs and Trade (GATT), and the efficacy of the provision in encouraging domestic manufacturing for manufacturers who do not file Paragraph IV challenges. GPhA would like to continue to discuss the specific questions posed in the discussion draft with the Committee.

Clinical Trial Reform

GPhA supports the discussion document's goal of modernizing and reforming clinical trials. By accelerating the development phase of the prescription drug cycle, we can spur new cures for patients and our manufacturers can sooner bring cost-saving generic versions onto the market.

Conclusion

GPhA and its member companies will continue our review of the discussion draft and will provide the Committee additional comments that we look forward to discussing. We share a common goal to ensure that our nation's drug and device discovery, development approval infrastructure and processes are structured to find the cures we need, encourage innovation, and deliver treatments to patients. We will work with the Committee to improve select provisions, so that the final 21st Century Cures document reflects the important role that competition plays in spurring innovation, promoting competition, and ensuring access to affordable medicines.

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[i] Testimony of C. Scott Hemphill, Professor of Law, Columbia Law School, House Committee on Energy and Commerce Subcommittee on Health Hearing on 21st Century Cures: Examining the Role of Incentives in Advancing Treatments and Cures for Patients, June 11, 2014.